120311

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: RITA MITRA Examiner #: 77995 Date: 04/23/04
Art Unit: 1653 Phone Number 30 20954 Serial Number: 09/991588
Mail Box and Bldg. Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: "Composition and method of bone regeneration"

Inventors (please provide full names): JOHN ARNOLD BUDNY

Earliest Priority Filing Date: 07/24/1998

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

I would request an expedited text search (both patent and Non-patent literature) for this application, because I intend to ~~search~~ submit the case this biweek. Please read the abstract, which should be covered in the search. Please focus on ~~the~~ "Osteonectin and SPARC" only from the list of protein recited in claims 3 & 5. Ignore other proteins and sequences. This is not a Seq. srch request.

Keywords:
matrix
fibronectin
Osteoblast activity
Osteoclast
Vitronectin
Osteonectin
SPARC (Secreted protein acidic and rich in Cysteine)

Please do an author search also

Rush Search Approved
Thurman K Page
SPE, AU 1615

STAFF USE ONLY

Searcher: _____
Searcher Phone #: _____

Type of Search
NA Sequence (#) _____
AA Sequence (#) _____

Vendors and cost where applicable
STN _____

```
=> file hcaplus; d que l5
FILE 'HCAPLUS' ENTERED AT 14:09:42 ON 27 APR 2004
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FILE COVERS 1907 - 27 Apr 2004  VOL 140 ISS 18
FILE LAST UPDATED: 26 Apr 2004  (20040426/ED)
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L3            34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BUDNY J?/AU
L4             4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND BONE
L5             2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 NOT DOGS/TI

=> file medline; d que l39
FILE 'MEDLINE' ENTERED AT 14:09:57 ON 27 APR 2004
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FILE LAST UPDATED: 24 APR 2004 (20040424/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L39            0 SEA FILE=MEDLINE ABB=ON  PLU=ON  (BUDNY JA OR BUDNY JOHN A OR
                 BUDNY JOHN ARNOLD)/AU

=> file embase; d que l81
FILE 'EMBASE' ENTERED AT 14:10:05 ON 27 APR 2004
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FILE COVERS 1974 TO 22 Apr 2004 (20040422/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

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substance identification.

```
L80             5 SEA FILE=EMBASE ABB=ON  PLU=ON  BUDNY J/AU NOT BUDNY J L/AU
L81             0 SEA FILE=EMBASE ABB=ON  PLU=ON  L80 AND BONE


=> file biosis; d que l115
FILE 'BIOSIS' ENTERED AT 14:10:12 ON 27 APR 2004
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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 April 2004 (20040421/ED)

FILE RELOADED: 19 October 2003.


L114            7 SEA FILE=BIOSIS ABB=ON  PLU=ON  BUDNY J A/AU OR BUDNY JOHN
                  A/AU
L115            0 SEA FILE=BIOSIS ABB=ON  PLU=ON  L114 AND BONE


=> file wpix; d que l117
FILE 'WPIX' ENTERED AT 14:10:20 ON 27 APR 2004
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FILE LAST UPDATED:          26 APR 2004      <20040426/UP>
MOST RECENT DERWENT UPDATE:     200427        <200427/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
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    http://thomsonderwent.com/coverage/latestupdates/          <<<

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>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
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>>> THE DISPLAY LAYOUT HAS BEEN CHANGED TO ACCOMODATE THE
    NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION
    NUMBERS. SEE ALSO:
    http://www.stn-international.de/archive/stnews/news0104.pdf <<<
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>>> SINCE THE FILE HAD NOT BEEN UPDATED BETWEEN APRIL 12-16
THERE WAS NO WEEKLY SDI RUN <<<

L116 10 SEA FILE=WPIX ABB=ON PLU=ON BUDNY J?/AU
L117 2 SEA FILE=WPIX ABB=ON PLU=ON L116 AND BONE

=> dup rem l5 l117
FILE 'HCAPLUS' ENTERED AT 14:10:47 ON 27 APR 2004
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PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L117
L133 2 DUP REM L5 L117 (2 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE HCAPLUS

=> d ibib ab l133 1-2

L133 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:930732 HCAPLUS
DOCUMENT NUMBER: 139:386446
TITLE: Composition and method for **bone** regeneration
INVENTOR(S): **Budny, John Arnold**
PATENT ASSIGNEE(S): Pharmacal Biotechnologies, Llc, USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 122,348, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003219429	A1	20031127	US 2001-991588	20011121
PRIORITY APPLN. INFO.:			US 1998-122348 B2	19980724

AB A composition for modulating **bone** regeneration composition comprises a matrix selected from the group consisting of glycolic acid, lactic acid, collagen, demineralized **bone**, or a combination thereof. A first biol. active mol. comprising a fibronectin is attached to a portion of the matrix, to facilitate osteoblast activity and for promoting an increase in **bone** formation. A second biol. active mol. comprising a vitronectin, selected for its ability to attract osteoclasts and produce an inhibiting effect on osteoclast activity to thereby promote a decrease in **bone** resorption, is also attached to a portion of the matrix.

L133 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2000:84662 HCAPLUS
DOCUMENT NUMBER: 132:142003
TITLE: Osseous tissue reconstruction system containing polymer scaffolds
INVENTOR(S): **Budny, John A.**
PATENT ASSIGNEE(S): Pharmacal Biotechnologies, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004941	A1	20000203	WO 1999-US16800	19990722
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9953906	A1	20000214	AU 1999-53906	19990722
EP 1100558	A1	20010523	EP 1999-939654	19990722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003513682	T2	20030415	JP 2000-560932	19990722

PRIORITY APPLN. INFO.: US 1998-122348 A 19980724
WO 1999-US16800 W 19990722

AB An osseous tissue reconstruction system comprises a first component including a scaffold and a biol. active mol. attached for promoting an increase in **bone** formation, and a second component for promoting a decrease in **bone** resorption. Thus, carboxyl-terminated polyester e.g., poly(L-lactic acid) of varying mole-percent compns. of monomers and mol. wts. are derivatized at the free carboxyl groups with amino,groups associated with a biol. active peptide. The compound stimulates new **bone** synthesis, and inhibits **bone** resorption and loss.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=>  file hcaplus; d que l33; d que l34; d que l38
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FILE COVERS 1907 - 27 Apr 2004  VOL 140 ISS 18
FILE LAST UPDATED: 26 Apr 2004  (20040426/ED)

 This file contains CAS Registry Numbers for easy and accurate
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L6          5777 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE FORMATION+PFT/CT
L7         62803 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE+PFT/CT
L8          4603 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE MORPHOGENETIC PROTEINS+PF
                 T/CT
L9          8213 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OSTEOBLAST+OLD/CT
L12         8139 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLYCOLIC ACID+PFT/CT
L13         1039 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLYCOLIC ACID, BIOLOGICAL
                 STUDIES
L14        47458 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTIC ACID+PFT/CT
L15        14225 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTIC ACID, BIOLOGICAL
                 STUDIES
L16        53407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COLLAGENS+PFT/CT
L17        40254 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COLLAGENS, BIOLOGICAL STUDIES

L19       447920 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MATRIX
L20        14656 SEA FILE=HCAPLUS ABB=ON  PLU=ON  FIBRONECTINS/CT
L26          818 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OSTEONECTIN+PFT/CT
L27          624 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SPARC
L28          216 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SECRETED PROTEIN (5W)
                 CYSTEINE
L30           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L6 OR L7 OR L8 OR L9) AND
                 L19 AND ((L12 OR L13) OR (L14 OR L15) OR (L16 OR L17)) AND L20
                 AND (L26 OR L27 OR L28)
L32        12633 SEA FILE=HCAPLUS ABB=ON  PLU=ON  EXTRACELLULAR MATRIX+PFT/CT
L33           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 AND L32



L6          5777 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE FORMATION+PFT/CT
L7         62803 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE+PFT/CT
L8          4603 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE MORPHOGENETIC PROTEINS+PF
                 T/CT
L9          8213 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OSTEOBLAST+OLD/CT
L12         8139 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLYCOLIC ACID+PFT/CT
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L13          1039 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLYCOLIC ACID, BIOLOGICAL
                  STUDIES
L14         47458 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTIC ACID+PFT/CT
L15         14225 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTIC ACID, BIOLOGICAL
                  STUDIES
L16         53407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COLLAGENS+PFT/CT
L17         40254 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COLLAGENS, BIOLOGICAL STUDIES

L19        447920 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MATRIX
L20         14656 SEA FILE=HCAPLUS ABB=ON  PLU=ON  FIBRONECTINS/CT
L26           818 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OSTEONECTIN+PFT/CT
L27           624 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SPARC
L28           216 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SECRETED PROTEIN (5W)
                  CYSTEINE
L30            32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L6 OR L7 OR L8 OR L9) AND
                  L19 AND ((L12 OR L13) OR (L14 OR L15) OR (L16 OR L17)) AND L20
                  AND (L26 OR L27 OR L28)
L34             6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 AND (IMPLANT OR TRANSFORM?
                   OR MINERALIZ? OR CALVAR?)/TI



L6           5777 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE FORMATION+PFT/CT
L7          62803 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE+PFT/CT
L8           4603 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BONE MORPHOGENETIC PROTEINS+PF
                  T/CT
L9           8213 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OSTEOBLAST+OLD/CT
L12          8139 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLYCOLIC ACID+PFT/CT
L13          1039 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLYCOLIC ACID, BIOLOGICAL
                  STUDIES
L14         47458 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTIC ACID+PFT/CT
L15         14225 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTIC ACID, BIOLOGICAL
                  STUDIES
L16         53407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COLLAGENS+PFT/CT
L17         40254 SEA FILE=HCAPLUS ABB=ON  PLU=ON  COLLAGENS, BIOLOGICAL STUDIES

L19        447920 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MATRIX
L20         14656 SEA FILE=HCAPLUS ABB=ON  PLU=ON  FIBRONECTINS/CT
L21          1911 SEA FILE=HCAPLUS ABB=ON  PLU=ON  VITRONECTIN+PFT/CT
L24           646 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RGD PEPTIDES+PFT/CT
L25          8688 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SIALOGLYCOPROTEINS+PFT/CT
L26           818 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OSTEONECTIN+PFT/CT
L27           624 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SPARC
L28           216 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SECRETED PROTEIN (5W)
                  CYSTEINE
L30            32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L6 OR L7 OR L8 OR L9) AND
                  L19 AND ((L12 OR L13) OR (L14 OR L15) OR (L16 OR L17)) AND L20
                  AND (L26 OR L27 OR L28)
L36            50 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L6 OR L7 OR L8 OR L9) AND
                  (L24 OR L25 OR L26 OR L27 OR L28) AND L19 AND ((L12 OR L13) OR
                  (L14 OR L15) OR (L16 OR L17)) AND (L20 OR L21)
L37            18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 NOT L30
L38            14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L37 NOT (OSTEOM? OR CSF OR
                  CERAMIC OR PHENOTYPE)/TI

=> s (l33 or l34 or l38) not l5
L134           30 (L33 OR L34 OR L38) NOT L5   L5 = inventors, previously displayed

=> file medline; d ue 153; d que 162; d que 164
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FILE 'MEDLINE' ENTERED AT 14:12:22 ON 27 APR 2004

FILE LAST UPDATED: 24 APR 2004 (20040424/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

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L53 HAS NO ANSWERS

L40	16065	SEA FILE=MEDLINE ABB=ON	PLU=ON	OSTEOGENESIS/CT OR BONE DEVELOPMENT/CT
L41	4109	SEA FILE=MEDLINE ABB=ON	PLU=ON	BONE MORPHOGENETIC PROTEINS/CT
L43	1198	SEA FILE=MEDLINE ABB=ON	PLU=ON	GLYCOLIC ACID
L44	22055	SEA FILE=MEDLINE ABB=ON	PLU=ON	LACTIC ACID
L45	59112	SEA FILE=MEDLINE ABB=ON	PLU=ON	COLLAGEN+NT/CT
L46	21967	SEA FILE=MEDLINE ABB=ON	PLU=ON	FIBRONECTINS/CT OR LAMININ/CT OR TENASCIN/CT OR VITRONECTIN/CT
L47	887	SEA FILE=MEDLINE ABB=ON	PLU=ON	OSTEONECTIN/CT OR SPARC
L53	0	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L40 OR L41) AND (L43 OR L44 OR L45) AND L46 AND L47

L40	16065	SEA FILE=MEDLINE ABB=ON	PLU=ON	OSTEOGENESIS/CT OR BONE DEVELOPMENT/CT
L41	4109	SEA FILE=MEDLINE ABB=ON	PLU=ON	BONE MORPHOGENETIC PROTEINS/CT
L51	13843	SEA FILE=MEDLINE ABB=ON	PLU=ON	EXTRACELLULAR MATRIX/CT
L57	686	SEA FILE=MEDLINE ABB=ON	PLU=ON	OSTEONECTIN/CT
L58	351	SEA FILE=MEDLINE ABB=ON	PLU=ON	L57/MAJ
L62	1	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L40 OR L41) AND L58 AND L51

L40	16065	SEA FILE=MEDLINE ABB=ON	PLU=ON	OSTEOGENESIS/CT OR BONE DEVELOPMENT/CT
L41	4109	SEA FILE=MEDLINE ABB=ON	PLU=ON	BONE MORPHOGENETIC PROTEINS/CT
L51	13843	SEA FILE=MEDLINE ABB=ON	PLU=ON	EXTRACELLULAR MATRIX/CT
L63	500	SEA FILE=MEDLINE ABB=ON	PLU=ON	SPARC
L64	0	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L40 OR L41) AND L63 AND L51

=> file embase; d que l89
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```
L65          5839 SEA FILE=EMBASE ABB=ON  PLU=ON  BONE DEVELOPMENT/CT
L66          1501 SEA FILE=EMBASE ABB=ON  PLU=ON  BONE MATURATION/CT
L67          4820 SEA FILE=EMBASE ABB=ON  PLU=ON  OSTEOGENESIS
L68         13840 SEA FILE=EMBASE ABB=ON  PLU=ON  OSTEOBLAST?
L69          2598 SEA FILE=EMBASE ABB=ON  PLU=ON  BONE MORPHOGENETIC PROTEIN/CT
L70          1906 SEA FILE=EMBASE ABB=ON  PLU=ON  GLYCOLIC ACID
L71         27290 SEA FILE=EMBASE ABB=ON  PLU=ON  LACTIC ACID
L72         49472 SEA FILE=EMBASE ABB=ON  PLU=ON  COLLAGEN+NT/CT
L73         15081 SEA FILE=EMBASE ABB=ON  PLU=ON  FIBRONECTIN/CT
L74          7713 SEA FILE=EMBASE ABB=ON  PLU=ON  LAMININ/CT
L75          1707 SEA FILE=EMBASE ABB=ON  PLU=ON  TENASCIN/CT
L76          2159 SEA FILE=EMBASE ABB=ON  PLU=ON  VITRONECTIN/CT
L77           750 SEA FILE=EMBASE ABB=ON  PLU=ON  OSTEONECTIN/CT
L78           492 SEA FILE=EMBASE ABB=ON  PLU=ON  SPARC OR (SECRETED PROTEIN)
                  (5W) CYSTEINE
L85         22494 SEA FILE=EMBASE ABB=ON  PLU=ON  EXTRACELLULAR MATRIX+NT/CT
L86            33 SEA FILE=EMBASE ABB=ON  PLU=ON  (L65 OR L66 OR L67 OR L68 OR
                  L69) AND (L70 OR L71 OR L72 OR L73 OR L74 OR L75 OR L76) AND
                  (L77 OR L78) AND L85
L88            10 SEA FILE=EMBASE ABB=ON  PLU=ON  L86 AND (ENGINEER? OR BIOMATER?
                   OR PROLIFE? OR SCULPT OR REMODEL? OR OSTEOGL?)/TI
L89             7 SEA FILE=EMBASE ABB=ON  PLU=ON  L88 NOT (ECTOPIC OR MECHANO?
                  OR ANEURYSM)/TI
```

```
=> file biosis; d que l113
FILE 'BIOSIS' ENTERED AT 14:12:39 ON 27 APR 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 April 2004 (20040421/ED)

FILE RELOADED: 19 October 2003.
```

```
L90         27654 SEA FILE=BIOSIS ABB=ON  PLU=ON  BONE (2A) (DEVELOP? OR MATUR?
                  OR FORM? OR REGENERAT? OR MORPHOGENETIC OR MINERALIZ?)
L91         20705 SEA FILE=BIOSIS ABB=ON  PLU=ON  BONE (2A) (RESOR? OR DEMINERALI
                  Z?) OR OSTEOCLAST?
L92         19062 SEA FILE=BIOSIS ABB=ON  PLU=ON  (GLYCOLIC OR LACTIC) (W) ACID
L93        113789 SEA FILE=BIOSIS ABB=ON  PLU=ON  COLLAGEN? OR PROCOLLAGEN?
L94         28064 SEA FILE=BIOSIS ABB=ON  PLU=ON  FIBRONECTIN
L95         15669 SEA FILE=BIOSIS ABB=ON  PLU=ON  LAMININ
L96          2575 SEA FILE=BIOSIS ABB=ON  PLU=ON  TENASCIN
L97          3602 SEA FILE=BIOSIS ABB=ON  PLU=ON  VITRONECTIN
L98         24623 SEA FILE=BIOSIS ABB=ON  PLU=ON  INTEGRIN
L99           864 SEA FILE=BIOSIS ABB=ON  PLU=ON  OSTEONECTIN
L100          741 SEA FILE=BIOSIS ABB=ON  PLU=ON  SPARC OR (SECRETED PROTEIN)(5A)
                   CYSTEINE
L103       140052 SEA FILE=BIOSIS ABB=ON  PLU=ON  MATRIX
L104        36938 SEA FILE=BIOSIS ABB=ON  PLU=ON  EXTRACELLULAR MATRIX
L107           29 SEA FILE=BIOSIS ABB=ON  PLU=ON  L90 AND (L99 OR L100) AND L104
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L109          14 SEA FILE=BIOSIS ABB=ON  PLU=ON  L90 AND (L99 OR L100) AND (L92
                 OR L93) AND (L94 OR L95 OR L96 OR L97 OR L98) AND L103
L111          27 SEA FILE=BIOSIS ABB=ON  PLU=ON  L94 AND L97 AND L103 AND (L90
                 OR L91)
L112          26 SEA FILE=BIOSIS ABB=ON  PLU=ON  L111 NOT (L107 OR L109)
L113           3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L112 AND (SCAFFOLDS OR ANALOGS
                 OR ANORGANIC)/TI


=> file wpix; d que l128; d que l132
FILE 'WPIX' ENTERED AT 14:12:54 ON 27 APR 2004
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FILE LAST UPDATED:          26 APR 2004      <20040426/UP>
MOST RECENT DERWENT UPDATE:     200427        <200427/DW>
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    NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION
    NUMBERS. SEE ALSO:
    http://www.stn-international.de/archive/stnews/news0104.pdf <<<

>>> SINCE THE FILE HAD NOT BEEN UPDATED BETWEEN APRIL 12-16
    THERE WAS NO WEEKLY SDI RUN  <<<


L118       46311 SEA FILE=WPIX ABB=ON  PLU=ON  BONE OR OSTEOGENESIS OR OSTEOBLAS
                 T?
L119        1485 SEA FILE=WPIX ABB=ON  PLU=ON  FIBRONECTIN
L120         430 SEA FILE=WPIX ABB=ON  PLU=ON  VITRONECTIN
L121         110 SEA FILE=WPIX ABB=ON  PLU=ON  OSTEONECTIN OR SPARC OR (SECRETED
                  PROTEIN) (5A) CYSTEINE
L123        1909 SEA FILE=WPIX ABB=ON  PLU=ON  OSTEOCLAST OR BONE (2A) RESOR?
L124      138009 SEA FILE=WPIX ABB=ON  PLU=ON  MATRIX
L126           9 SEA FILE=WPIX ABB=ON  PLU=ON  (L118 OR L123) AND (L119 OR
                 L120) AND L121 AND L124
L127           7 SEA FILE=WPIX ABB=ON  PLU=ON  L126 AND (REPAIR? OR DEVICE OR
                 PROMOTER OR BIOACTIVE OR CULTUR?)/TI
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L128          6 SEA FILE=WPIX ABB=ON  PLU=ON  L127 NOT ENDOMURAL/TI


L118      46311 SEA FILE=WPIX ABB=ON  PLU=ON  BONE OR OSTEOGENESIS OR OSTEOBLAS
                T?
L119       1485 SEA FILE=WPIX ABB=ON  PLU=ON  FIBRONECTIN
L120        430 SEA FILE=WPIX ABB=ON  PLU=ON  VITRONECTIN
L121        110 SEA FILE=WPIX ABB=ON  PLU=ON  OSTEONECTIN OR SPARC OR (SECRETED
                 PROTEIN) (5A) CYSTEINE
L123       1909 SEA FILE=WPIX ABB=ON  PLU=ON  OSTEOCLAST OR BONE (2A) RESOR?
L124     138009 SEA FILE=WPIX ABB=ON  PLU=ON  MATRIX
L125         13 SEA FILE=WPIX ABB=ON  PLU=ON  (L118 OR L123) AND (L119 OR
                L120) AND L121
L130         21 SEA FILE=WPIX ABB=ON  PLU=ON  L121 AND L124 AND (L118 OR L123)

L131         12 SEA FILE=WPIX ABB=ON  PLU=ON  L130 NOT (L125)
L132          4 SEA FILE=WPIX ABB=ON  PLU=ON  L131 NOT ( MICROARRAY OR
                FUMARATE OR REPEATING OR PHOSPHATE OR GRAFT SUBSTITUTE OR
                SHAPED)/TI


=> s (l128 or l132) not l117
L135          9 (L128 OR L132) NOT L117  L117 = inventors, previously displayed

=> dup rem l62 l134 l89 l113 l135
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FILE 'HCAPLUS' ENTERED AT 14:14:15 ON 27 APR 2004
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COPYRIGHT (C) 2004 THOMSON DERWENT
PROCESSING COMPLETED FOR L62
PROCESSING COMPLETED FOR L134
PROCESSING COMPLETED FOR L89
PROCESSING COMPLETED FOR L113
PROCESSING COMPLETED FOR L135
L136         48 DUP REM L62 L134 L89 L113 L135 (2 DUPLICATES REMOVED)
                ANSWER '1' FROM FILE MEDLINE
                ANSWERS '2-31' FROM FILE HCAPLUS
                ANSWERS '32-37' FROM FILE EMBASE
                ANSWERS '38-40' FROM FILE BIOSIS
                ANSWERS '41-48' FROM FILE WPIX

=> d ibib ab l136 1-40; d ibib ab abex l136 41-48

L136 ANSWER 1 OF 48     MEDLINE on STN
ACCESSION NUMBER:    95374746     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 7646875
TITLE:               Cultured tibial rat osteoblasts: in vitro production and
                     topography of osteonectin, biglycan and decorin.
```

AUTHOR: Puddu A; Filanti C; Zicca A; Cadoni A; Manduca P
CORPORATE SOURCE: Istituto di Fisiologia Universita di Genova.
SOURCE: Bollettino della Societa italiana di biologia sperimentale, (1995 Mar-Apr) 71 (3-4) 91-7.
Journal code: 7506962. ISSN: 0037-8771.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19951005
Last Updated on STN: 19951005
Entered Medline: 19950922

AB Rat osteoblasts in culture undergo differentiative changes culminating in the formation of mineralized foci. We here report on the pattern of temporal expression and compartmentalization of osteonectin and of the two small proteoglycans, byglican and decorin. They were constitutively synthesized during in vitro differentiation of rat osteoblasts. The 3 proteins were detected in the conditioned medium and associated with the cell-matrix compartment. Within this compartment they showed prevalent cytoplasmic location and differential distribution on unmineralized noduli was detected for osteonectin and byglican, while decorin was detected throughout the nodules. Along with known functions in the matrix, a possible role in the cytoplasm may have to be sought for these bone cells components.

L136 ANSWER 2 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:26059 HCAPLUS
DOCUMENT NUMBER: 139:219171
TITLE: Extracellular **matrix** production by human osteoblasts cultured on biodegradable polymers applicable for tissue engineering
AUTHOR(S): El-Amin, S. F.; Lu, H. H.; Khan, Y.; Burems, J.; Mitchell, J.; Tuan, R. S.; Laurencin, C. T.
CORPORATE SOURCE: Department of Chemical Engineering, Center for Advanced Biomaterials and Tissue Engineering, Drexel University, Philadelphia, PA, 19104, USA
SOURCE: Biomaterials (2003), 24(7), 1213-1221
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The nature of the extracellular **matrix** (ECM) is crucial in regulating cell functions via cell-**matrix** interactions, cytoskeletal organization, and integrin-mediated signaling. In bone, the ECM is composed of proteins such as collagen (CO), fibronectin (FN), laminin (LM), vitronectin (VN), osteopontin (OP) and osteonectin (ON). For bone tissue engineering, the ECM should also be considered in terms of its function in mediating cell adhesion to biomaterials. This study examined ECM production, cytoskeletal organization, and adhesion of primary human osteoblastic cells on biodegradable **matrixes** applicable for tissue engineering, namely polylactic-co-glycolic acid 50:50 (PLAGA) and polylactic acid (PLA). We hypothesized that the osteocompatible, biodegradable polymer surfaces promote the production of bone-specific ECM proteins in a manner dependent on polymer composition We first examined whether the PLAGA and PLA **matrixes** could support human osteoblastic cell growth by measuring cell adhesion at 3, 6 and 12 h post-plating. Adhesion on PLAGA was consistently higher than on PLA throughout the duration of the experiment, and comparable to tissue culture polystyrene (TCPS). ECM components, including CO, FN, LM, ON, OP and VN, produced on the surface

of the polymers were quantified by ELISA and localized by immunofluorescence staining. All of these proteins were present at significantly higher levels on PLAGA compared to PLA or TCPS surfaces. On PLAGA, OP and ON were the most abundant ECM components, followed by CO, FN, VN and LN. Immunofluorescence revealed an extracellular distribution for CO and FN, whereas OP and ON were found both intracellularly as well as extracellularly on the polymer. In addition, the actin cytoskeletal network was more extensive in osteoblasts cultured on PLAGA than on PLA or TCPS. In summary, we found that osteoblasts plated on PLAGA adhered better to the substrate, produced higher levels of ECM mols., and showed greater cytoskeletal organization than on PLA and TCPS. We propose that this difference in ECM composition is functionally related to the enhanced cell adhesion observed on PLAGA. There is initial evidence that specific composition of the PLAGA polymer favors the ECM. Future studies will seek to optimize ECM production on these **matrixes** for bone tissue engineering applications.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 3 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2001:676616 HCAPLUS
DOCUMENT NUMBER: 135:231740
TITLE: **Implant** product comprising a **matrix** and a protein mixture and its use for anchoring connective tissue to bone
INVENTOR(S): Atkinson, Brent; Benedict, James J.
PATENT ASSIGNEE(S): Sulzer Biologics Inc., USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066130	A1	20010913	WO 2001-US7130	20010307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1261365	A1	20021204	EP 2001-918377	20010307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-523923 A 20000309
WO 2001-US7130 W 20010307

AB Disclosed is a product that enhances an attachment of connective tissue to bone. Also disclosed is a method of regenerating and repairing attachments of connective tissue to bone using such a product. The product comprises: a. a **matrix** configured to interface between connective tissue and bone; and b. a composition comprising a mixture of proteins associated with the **matrix**. The mixture of proteins comprises of at least: transforming growth factor β1, bone morphogenetic protein (BMP)-2, BMP-3, and BMP-7. The **matrix** is bioresorbable, porous, and comprises a material selected from the group consisting of a synthetic

polymeric material, a ground substance, a sponge, a membrane, a film or a gel.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 4 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173752 HCAPLUS
DOCUMENT NUMBER: 138:215251
TITLE: Screening assays for identifying differentiation-inducing agents, and production of differentiated cells for cell therapy
INVENTOR(S): West, Michael D.; Page, Raymond; Scholer, Hans; Chapman, Karen
PATENT ASSIGNEE(S): Advanced Cell Technology, Inc., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018760	A2	20030306	WO 2002-US26945	20020826
WO 2003018760	A3	20030821		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003224345	A1	20031204	US 2002-227282	20020826
			US 2001-314316P P	20010824

PRIORITY APPLN. INFO.:

AB The invention relates to assays for screening growth factors, adhesion mols., immunostimulatory mols., extracellular **matrix** components and other materials, alone or in combination, simultaneously or temporally, for the ability to induce directed differentiation of pluripotent and multipotent stem cells.

L136 ANSWER 5 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:350786 HCAPLUS
DOCUMENT NUMBER: 139:177379
TITLE: Early expression of bone **matrix** proteins in osteogenic cell cultures
AUTHOR(S): Tambasco de Oliveira, Paulo; Zalzal, Sylvia Francis; Irie, Kazuharu; Nanci, Antonio
CORPORATE SOURCE: Laboratory for the Study of Calcified Tissues and Biomaterials, Faculty of Dentistry, Universite de Montreal, Montreal, QC, Can.
SOURCE: Journal of Histochemistry and Cytochemistry (2003), 51(5), 633-641
CODEN: JHCYAS; ISSN: 0022-1554
PUBLISHER: Histochemical Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Osteogenic cells express some **matrix** proteins at early culture intervals. The aim of this study was to determine if, and in what proportion, cells used for plating contain bone sialoprotein (BSP) and osteopontin (OPN), two **matrix** proteins associated with initial events in bone formation. Their pattern of expression, as well as that of fibronectin (FN) and type I pro-collagen, was also examined at 6 h and at 1 and 3 days. The cells were obtained by enzymic digestion of newborn rat calvariae, and grown on glass coverslips. Cytocentrifuge prepns. of isolated cells and coverslips were processed for single or dual immunolabeling with monoclonal and/or polyclonal primary antibodies, followed by fluorochrome-conjugated antibodies. The cell labeling was mainly associated with perinuclear elements. OPN was also distinctively found at peripheral cytoplasmic sites. About 31% of isolated cells were OPN-pos. and 18% were BSP-pos. After 1 day, almost 50% of cells were immunoreactive for OPN and for type I pro-collagen, and still less than 20% reacted for BSP. Approx. 7% exhibited peripheral staining for OPN. Almost all cells were associated with extracellular FN. However, only 15% showed intracellular labeling. These results indicate that an important proportion of cells used for plating contain BSP and OPN, a situation that should be taken into consideration in exptl. analyses of osteoblast activity in vitro.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 6 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:978584 HCAPLUS
DOCUMENT NUMBER: 138:34125
TITLE: Determining changes in phenotype-specific gene expression in a cell by measuring changes in housekeeping and phenotype-specific gene expression
INVENTOR(S): Nishimura, Ichiro; Iida, Keisuke
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002197640	A1	20021226	US 2002-174658	20020619
WO 2004000867	A1	20031231	WO 2002-US19705	20020731

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-299910P P 20010621
US 2002-174658 A 20020619

AB The present invention provides an improved method for assessing, monitoring and/or determining the phenotype of cells and tissues. One aspect of the present invention is a method of fabricating phenotype specific gene (PSGs) and house keeping gene (HKGs) targets onto a microarray. Another aspect of the present invention provides a composition containing PSGs and HKGs as

targets for high throughput assays including microarray analyses. Another aspect of the present invention is accessing, monitoring and/or determining the phenotype of tissue engineered cells derived from stem cells including embryonic stem cells, embryonic germ cells, fetal stem cells and adult stem cells by hybridizing cDNA probes to either PSG or HKG targets. These methods employ at least 25 PSG targets and no greater than 5000 HKG targets. Specific genes for use in measuring changes in given tissues are claimed.

L136 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:143320 HCAPLUS
DOCUMENT NUMBER: 136:189420
TITLE: Tissue engineering composite for purposes of repairing damaged tissues and reconstructing new tissues
INVENTOR(S): Burg, Karen J. L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002022883	A1	20020221	US 2001-879360	20010612
PRIORITY APPLN. INFO.:			US 2000-211147P P	20000613

AB The invention provides a biocompatible composite for use in a living subject for purposes of repairing damaged tissues and reconstructing a new tissue. The composite includes a biodegradable or absorbable three-dimensional support construct, a liquid or viscous fluid forming a gel **matrix** or viscous fluid when delivered to an area of interest in a living subject. The biodegradable construct provides an ideal surface for cell or cell extract attachment, while the gel **matrix** or viscous fluid acts as both a carrier material and a separator for maintaining the space between the constructs as well as the structural integrity of the developing issue. Collagen beads were dynamically loaded for 48 h with rat aortic smooth muscle cells, then were mixed and gelled in alginates of 0.5, 1.0, and 2.0% gel strengths following cultivation. Composites were similarly prepared and 1 mL of the composite was injected s.c. in each exptl. female Lewis rat. Samples were retrieved after 2, 4, and 6 wk and assessed histol. using a series of cell-specific stains. The in vitro studies demonstrated that the 2.0 percent gel did not allow the high cell viabilities and the low gel strength of 0.5 percent did not maintain the necessary polymeric form. The in vivo work demonstrated that the material can be readily injected and thus is clin. feasible. All composites showed minimal inflammation and minimal fibrous encapsulation, and they appeared to be able to readily conform to irregular defects.

L136 ANSWER 8 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:833138 HCAPLUS
DOCUMENT NUMBER: 135:376822
TITLE: Polymer-based medical **implant** materials
INVENTOR(S): Griffin, Martin; Heath, Deborah; Christian, Paul
PATENT ASSIGNEE(S): The Nottingham Trent University, UK
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085224	A1	20011115	WO 2001-GB1910	20010502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1280563	A1	20030205	EP 2001-925694	20010502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004030408	A1	20040212	US 2003-276230	20030709
PRIORITY APPLN. INFO.:			GB 2000-11356 A	20000512
			WO 2001-GB1910 W	20010502

AB The present invention provides a medical implant material comprising a mammalian transglutaminase and a polymer, wherein the transglutaminase is provided in the absence of free divalent metal ions and wherein the polymer is associated with the transglutaminase binding protein. Preferably, the transglutaminase is a tissue transglutaminase, which is coated on, impregnated into or covalently linked to the polymer. The polymer may be naturally occurring or synthetic, and may be biodegradable or non-biodegradable. The medical implant material may further comprise a reinforcing agent and/or one or more addnl. polymers. The invention further provides the use of a mammalian transglutaminase in a method for improving the biocompatibility of a medical implant material, the method comprising the steps of (i) providing a medical implant material comprising a polymer associated with a binding protein for binding the transglutaminase, and (ii) treating the material with a mammalian transglutaminase. Poly(ε-caprolactone) coated with fibronectin and tissue transglutaminase is a bioactive biomaterial that enhances cell attachment, spreading and stabilizes the extracellular **matrix** on the biomaterial surface making the human osteoblast-biomaterial interface stable. This biomaterial has potential applications in bone grafting where cells need to rapidly colonize the biomaterial in order to produce new bone. The PCL could also be re-enforced to give it the mech. strength required for hip and knee prosthesis.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 9 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:856498 HCAPLUS
DOCUMENT NUMBER: 137:129763
TITLE: Function of linear and cyclic RGD-containing peptides in osteoprogenitor cells adhesion process
AUTHOR(S): Verrier, S.; Pallu, S.; Bareille, R.; Jonczyk, A.; Meyer, J.; Dard, M.; Amedee, J.
CORPORATE SOURCE: Unite INSERM U 443, Bordeaux, F-33076, Fr.
SOURCE: Biomaterials (2001), Volume Date 2002, 23(2), 585-596
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cell adhesion directly influences cell growth, differentiation and migration as well as morphogenesis, integrity and repair. The

extracellular **matrix** (ECM) elaborated by osteoblast cells constitutes a regulator of the cell adhesion process and then of the related phenomenon. These regulatory effects of ECM are mediated through integrins and some of them are able to bind RGD sequences. The aim of this study was to determine the role of the sequence and the structure of RGD-containing peptides (linear and cyclic) as well as their role in the cell adhesion process. Cell adhesion assays onto ECM proteins coated surfaces were performed using a range of linear and cyclic RGD-containing peptides. The authors showed a different human osteoprogenitor cell adhesion according to the coating for ECM proteins and for RGD-peptides. Inhibition assays using peptides showed different responses depending on the coated protein. Depending on the amino-acid sequence and the structure of the peptides (cyclic/linear), 100% inhibition of cell adhesion onto vitronectin was observed These results suggest the importance of sequence, structure and conformation of the peptide, which may play a crucial function in the ligand/receptor interaction and/or in the stability of the interaction.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 10 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:93793 HCAPLUS
DOCUMENT NUMBER: 134:250126
TITLE: Bone mineralization and osteoblast differentiation are negatively modulated by integrin αvβ3
AUTHOR(S): Cheng, Su-Li; Lai, Chung-Fang; Blystone, Scott D.; Avioli, Louis V.
CORPORATE SOURCE: Division of Bone and Mineral Diseases, Washington University School of Medicine, St. Louis, MO, USA
SOURCE: Journal of Bone and Mineral Research (2001), 16(2), 277-288
CODEN: JBMREJ; ISSN: 0884-0431
PUBLISHER: American Society for Bone and Mineral Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Numerous bone **matrix** proteins can interact with αv-containing integrins including αvβ3. To elucidate the net effects of the interaction between these proteins and αvβ3 on osteoblast function, we developed a murine osteoblastic cell line that overexpressed human αvβ3. Human αvβ3-integrin was expressed on cell membrane, in which its presence did not alter the surface level of endogenous mouse αvβ3. The expressed human αvβ3 was functional because cell adhesion to osteopontin was increased and this increment was abolished by antibody against human αvβ3. The proliferation rate of cells overexpressing αvβ3 (αvβ3-cells) was increased whereas **matrix** mineralization was decreased. To elucidate the mechanisms leading to inhibition of **matrix** mineralization, the expression of proteins important for mineralization was analyzed. Alkaline phosphatase activity and the expression of osteocalcin, type I collagen, and bone sialoprotein (BSP) were decreased whereas osteopontin was stimulated in αvβ3-cells. The regulation of osteopontin, osteocalcin, and BSP expression was mediated via transcriptional mechanism because their promoter activities were altered. Examination of mols. involved in integrin signaling indicated that activator protein-1 (AP-1) and extracellular signal-regulated kinase (Erk) activities were enhanced whereas c-jun N-terminal kinase (JNK) activity was decreased in αvβ3-cells. The activity of p38 and the levels of focal adhesion kinase (FAK) and vinculin were not altered. Moreover, the adhesions of αvβ3-cells to type I collagen and fibronectin were inhibited,

which was attributed to decreased β1-integrin levels on cell surface. In conclusion, overexpressing αvβ3-integrin in osteoblasts stimulated cell proliferation but retarded differentiation, which were derived via altered integrin-**matrix** interactions, signal transduction, and **matrix** protein expression.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 11 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:277295 HCAPLUS
DOCUMENT NUMBER: 137:44724
TITLE: Characterization of human bone cells in culture
AUTHOR(S): Toesca, A.; Pagnotta, A.; Specchia, N.
CORPORATE SOURCE: Institute of Human Anatomy, Catholic University, Rome, Italy
SOURCE: Italian Journal of Anatomy and Embryology (2001), 106(1), 13-26
CODEN: IEMBEF; ISSN: 1122-6714
PUBLISHER: Editrice "Il Sedicesimo"
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Osteoblast-like cells isolated from human bone bioptic specimens were established in culture. Their osteoblast-like phenotype was studied by biochem., histochem. and immunohistochem. methods and by electron microscopy examination Third-passage cell cultures exhibited high level of alkaline phosphatase activity and the exposure to human parathyroid hormone produced an increase of intracellular cAMP. Cultured cells were immunoreactive for type I and type III collagen, osteonectin, and fibronectin; when ascorbic acid and β-glycerophosphate were added, they synthesized a rich extracellular **matrix**. This characterization ensures the reliability of osteoblast-like cultures when they are used as exptl. models.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 12 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:847615 HCAPLUS
DOCUMENT NUMBER: 134:308464
TITLE: Capacitively coupled electric fields accelerate proliferation of osteoblast-like primary cells and increase bone extracellular **matrix** formation in vitro
AUTHOR(S): Hartig, Mareke; Joos, Ulrich; Wiesmann, Hans-Peter
CORPORATE SOURCE: Klinik und Poliklinik fur Mund- und Kiefer-Gesichtschirurgie, Westfalische Wilhelms-Universitat, Munster, 48149, Germany
SOURCE: European Biophysics Journal (2000), 29(7), 499-506
CODEN: EBJOE8; ISSN: 0175-7571
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Over the last few years, elec. and electromagnetic fields have gained more and more significance in the therapy of bone fracture healing and bone disease. Yet, the underlying mechanisms on a cellular and mol. level are not completely understood. In the present study we have investigated the effects of capacitively coupled, pulsed elec. fields on cellular proliferation, alkaline phosphatase activity, and **matrix** protein synthesis of osteoblast-like primary cells in vitro. Cells were derived from bovine periosteum and elec. stimulated by saw-tooth pulses of 100 V external voltage and 16 Hz frequency. This corresponds to an elec. field

of 6 kV/m across the cell membranes as could be shown by computer simulation. Field application caused acceleration of cell culture development. A significant increase of proliferation concurrent with an enhancement of alkaline phosphatase activity was observed in sub-confluent cultures. Exposure of confluent osteoblast-like primary cells to elec. fields resulted in enhanced synthesis and secretion of extracellular **matrix**-related proteins. These findings suggest that capacitively coupled elec. fields accelerate bone cell proliferation and differentiation in vitro and enhance the synthesis of cells leading to promoted **matrix** formation and maturation.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 13 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:867123 HCAPLUS
DOCUMENT NUMBER: 134:144854
TITLE: Bone **matrix** proteins
AUTHOR(S): McKee, Marc D.; Sodek, Jaro
CORPORATE SOURCE: Faculty of Dentistry, McGill University, Montreal, QC, H3A 2B2, Can.
SOURCE: Osteoporosis Primer (2000), 46-63. Editor(s): Henderson, Janet E.; Goltzman, David. Cambridge University Press: Cambridge, UK.
CODEN: 69ASDQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review with 52 refs. Topics discussed include collagen; non-collagenous extracellular **matrix** proteins such as bone sialoprotein, osteopontin, osteonectin, bone acidic glycoprotein-75, osteocalcin, fibronectin, and small proteoglycans; and other proteins in the bone **matrix**.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 14 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:736893 HCAPLUS
DOCUMENT NUMBER: 131:332976
TITLE: Sustained dna delivery from structural porous **matrices** for gene therapy applications with special emphasis is on bone formation and regeneration
INVENTOR(S): Shea, Lonnie D.; Bonadido, Jeffrey; Mooney, David J.
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958656	A2	19991118	WO 1999-US10330	19990512
WO 9958656	A3	20000106		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BJ, BJ, CF, CG,

CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9938986	A1	19991129	AU 1999-38986		19990512
PRIORITY APPLN. INFO.:			US 1998-85305P	P	19980513
			US 1998-109054P	P	19981119
			WO 1999-US10330	W	19990512

AB Disclosed are particular 3-dimensional structural **matrixes** containing DNA and their use in the prolonged release of DNA in various biol. environments. The structural **matrix** is a porous polymer [PLGA]-based containing pores formed by gas foaming involving inert gases (CO2) and leaching out of a water-soluble particulate (salt, NACL, sugar, glucose, sucrose, mannitol) when exposed to body fluids. The admixt. is compression molded into a selected size and shape prior to executing the gas foaming process. The structural **matrix** may also be an alginate or modified alginate **matrix**. This structural **matrix** is a biocompatible or biodegradable **matrix**. It may also be a lactic acid polymer, glycolic acid polymer or lactic acid/glycolic acid copolymer **matrix**. At least part of this **matrix** may be comprised of lactic acid/glycolic acid (PLGA) copolymer **matrix**. The structural **matrix** may be modified where one side section is bonded to one cell interaction mol. such as cell adhesion mols., cell attachment peptides, proteoglycan attachment peptide sequences, proteoglycans, cell adhesion polysaccharides, growth factors, cell adhesion enzymes, RGD peptide, fibronectin, vitronectin, Laminin A, Laminin B1, Laminin B2, collagen 1 and thrombospondin. The DNA-**matrix** materials are created such that they maintain a defined space, allowing cellular migration, transfection and proliferation to occur in a controlled manner. Such DNA-containing structural **matrixes** are thus particularly useful in in vivo cell transfection and gene expression in the context of gene therapy. This may encode a protein for stimulating bone progenitors or wound healing in fibroblast or in tissue or organ regeneration or transplantation or an antigen for immunity or cytotoxic or apoptosis-inducing protein or a transcription factor or elongation factor or cell cycle control protein or kinase or phosphatase or DNA repair protein or oncogene or tumor suppressor or angiogenic protein or anti-angiogenic protein or immune response stimulating protein or cell surface receptor or accessory signaling mol. or transport protein or anti-bacterial or anti-viral protein or hormone or neurotransmitter or growth factor or growth factor receptor or interferon or interleukin or chemokine or cytokine or colony stimulating factor or chemotactic factor protein of growth hormone or parathyroid hormone or PTH1-34 polypeptide or bone morphogenic protein or BMP-2A or BMP-2B or BMP-3 or BMP-4 or BMP-5 or BMP-6 or BMP-7 or BMP-8 or TGF-α or TGF-β1 or TGF-β2 or latent TGFβ binding protein or activin/inhibin protein or FGF or GMCSF or EGF or PDGF or insulin-like growth factor or leukemia inhibitory factor. This method allows for the use in gene transfer to cells within a tissue site and in manufacture of a medicament for gene therapy. Implantable medical devices comprising this gene-**matrix** are described. The release of nucleic acids from the **matrix** is controlled by diffusion. This method also applies to cancer therapy or treating viral infection.

L136 ANSWER 15 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1999:77465 HCAPLUS
DOCUMENT NUMBER:	130:144173
TITLE:	Delivery of agents and method for regeneration of periodontal tissues
INVENTOR(S):	Jernberg, Gary R.
PATENT ASSIGNEE(S):	USA
SOURCE:	PCT Int. Appl., 20 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9903487	A1	19990128	WO 1998-US14707	19980716
W:	AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6123957	A	20000926	US 1997-895137	19970716
AU 9886584	A1	19990210	AU 1998-86584	19980716

PRIORITY APPLN. INFO.: US 1997-895137 A 19970716
WO 1998-US14707 W 19980716

AB The invention relates to a method of treating periodontal disease and related disorders to regenerate lost tissues, which includes the steps of: combining at least one tissue regenerative agent with at least one cellular recognition agent to form a therapeutic treatment composition and applying the therapeutic treatment composition to a periodontal treatment site. The cellular recognition agent increases the periodontal tissue regeneration at the periodontal treatment site relative to the therapeutic treatment composition lacking the cellular recognition agent. The invention also includes the therapeutic composition

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 16 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:680719 HCAPLUS
DOCUMENT NUMBER: 131:356058
TITLE: In vitro reactions of human osteoblasts in culture with zirconia and alumina ceramics
AUTHOR(S): Josset, Y.; Oum'Hamed, Z.; Zarrinpour, A.; Lorenzato, M.; Adnet, J. J.; Laurent-Maquin, D.
CORPORATE SOURCE: EA 2068, IFR 53, Centre d'Etude des Biomateriaux et Interfaces, Reims, 51000, Fr.
SOURCE: Journal of Biomedical Materials Research (1999), 47(4), 481-493
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The biocompatibility of two implantable materials, zirconia and alumina ceramics, was investigated in vitro by using human osteoblast cell cultures. The viability of osteoblast cells with the materials was evaluated by the methylthiazole sulfate test that revealed an absence of any cytostatic or cytotoxic effect. Cell proliferation kinetic and total protein synthesis in osteoblasts with zirconia or alumina were similar to that observed in control cells cultured on glass coverslips. Light and scanning electron microscopic examns. showed an intimate contact between osteoblasts and the substrates; well-spread cells were observed on the surfaces of both materials. Adhesion ability and morphol. characteristics were preserved in osteoblast cultures with these substrates. Moreover,

immunohistochem. staining in osteoblasts with zirconia and alumina showed the capacity of these cells to elaborate the extracellular **matrix** composed of types I and V collagen, osteocalcin, osteonectin, bone sialoprotein, and cellular fibronectin. Finally, DNA image cytometry and interphase silver-nucleolar organizer regions quantification were applied as complementary biocompatibility tests to detect any changes in DNA synthesis and cell proliferation, resp. Neither material altered cell ploidy or cell growth rate in accordance with the absence of any inducing effect on DNA synthesis or proliferation.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:245870 HCAPLUS
DOCUMENT NUMBER: 131:85946
TITLE: Selective attachment of osteoprogenitors to laminin
AUTHOR(S): Roche, P.; Goldberg, H. A.; Delmas, P. D.; Malaval, L.
CORPORATE SOURCE: INSERM Unite 403, Hopital E. Herriot, Lyon, Fr.
SOURCE: Bone (New York) (1999), 24(4), 329-336
CODEN: BONEDL; ISSN: 8756-3282
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During endochondral ossification and bone remodeling, osteoprogenitors (OP) attach to the **matrix** and differentiate into osteoblasts. To identify **matrix** proteins binding specifically these precursors, fetal rat calvaria (RC) cells were plated for 5-20 min in serum-free medium, on wells coated with various proteins and saturated with bovine serum albumin (BSA) to block nonspecific binding sites. Adherent cells were either counted or grown to assess bone colony (nodule) formation. As each nodule originates from the clonal division of one OP, the ratio (nodules/100 cells attached) measures the proportion of OP among adherent cells. Of numerous purified **matrix** proteins tested, laminin-1 and tenascin inhibited cell attachment, whereas fibronectin, bone sialoprotein, and type I collagen increased cell attachment and others had no effect. Only laminin-1 and, to a lesser extent, tenascin, enriched the cell population in OP. Laminin-1 acted time- and dose-dependently. In expts. in which cell attachment to laminin-coated but unsatd. wells was ensured by plating for 24 h in 10% fetal calf serum, laminin-1 had no effect on cell attachment nor on OP differentiation. In contrast, repeated plating of RC cells on laminin-1-coated/saturated wells depleted the population in OP, confirming that OP selection was a cell-attachment effect. When RC cell populations isolated by successive collagenase extns. were compared, the highest rate of OP enrichment on laminin-1 was obtained with the earliest populations, which were the most responsive to dexamethasone, a marker of early OP stages. In conclusion, laminin-1 recruits in vitro, through a cell-attachment effect, OP present in early RC cell populations, of which laminins are abundant extracellular **matrix** components.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:3293 HCAPLUS
DOCUMENT NUMBER: 130:61099
TITLE: Peptides for altering bone resorption, angiogenesis and restenosis
INVENTOR(S): Cheng, Soan; Ingram, Ronald; Mullen, Daniel; Tschopp, Juerg F.
PATENT ASSIGNEE(S): La Jolla Cancer Research Foundation, USA

SOURCE: U.S., 90 pp., Cont.-in-part of U.S. Ser. No. 303,052.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5849865	A	19981215	US 1995-421695	19950412
US 5770565	A	19980623	US 1994-303052	19940908
PRIORITY APPLN. INFO.:			US 1994-227316	19940413
			US 1994-303052	19940908

AB The invention provides Arg-Gly-Asp peptides that can alter the binding of osteoclasts to a **matrix** such as bone or can selectively alter integrin receptor binding. The invention also provides methods of using the Arg-Gly-Asp peptides to alter αvβ3 integrin receptor-mediated binding of a cell such as an osteoclast, endothelial cell or smooth muscle cell to a **matrix**. The invention further provides methods for ameliorating the severity of a pathol. characterized, in part, by an undesirable level of bone resorption, angiogenesis or restenosis in a subject.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 19 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:545397 HCAPLUS
DOCUMENT NUMBER: 129:170543
TITLE: Use of RGD peptides for altering bone resorption and integrin binding
INVENTOR(S): Cheng, Soan; Ingram, Ronald; Mullen, Daniel; Tschopp, Juerg F.
PATENT ASSIGNEE(S): La Jolla Cancer Research Center, USA
SOURCE: U.S., 88 pp., Cont.-in-part of U. S. 303,052.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5792745	A	19980811	US 1995-421697	19950412
US 5770565	A	19980623	US 1994-303052	19940908
PRIORITY APPLN. INFO.:			US 1994-227316	19940413
			US 1994-303052	19940908

OTHER SOURCE(S): MARPAT 129:170543
AB The invention provides Arg-Gly-Asp peptides that can alter the binding of osteoclasts to a **matrix** such as bone or can selectively alter integrin receptor binding. The invention also provides methods of using the Arg-Gly-Asp peptides to alter αvβ3 integrin receptor-mediated binding of a cell such as an osteoclast, endothelial cell, or smooth muscle cell to a **matrix**. The invention further provides methods for ameliorating the severity of a pathol. characterized, in part, by an undesirable level of bone resorption, angiogenesis or restenosis in a subject.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 20 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:17384 HCAPLUS
DOCUMENT NUMBER: 128:152169
TITLE: **Mineralization** and the expression of **matrix** proteins during in vivo bone development
AUTHOR(S): Cowles, E. A.; DeRome, M. E.; Pastizzo, G.; Brailey, L. L.; Gronowicz, G. A.
CORPORATE SOURCE: Dep. Orthopaedics, Univ. Connecticut Health Cent., Farmington, CT, 06032, USA
SOURCE: Calcified Tissue International (1998), 62(1), 74-82
CODEN: CTINDZ; ISSN: 0171-967X
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The in vivo expression of fibronectin, type I collagen, and several non-collagenous proteins was correlated with the development of bone in fetal and early neonatal rat calvariae. Fibronectin was the earliest **matrix** protein expressed in calvariae, with a peak expression in fetal 16- and 17-day (d) bones. Fibronectin expression coincided with the condensation of preosteoblasts prior to calcification and decreased once bone mineralization commenced. The expression of type I collagen, osteonectin, bone sialoprotein, and alkaline phosphatase mRNAs was found at 17 d. The increase in type I collagen mRNA levels was correlated with a 3.5-fold increase in calcium deposition at 19-20 d. Bone sialoprotein and alkaline phosphatase peaked on fetal 21 d while osteonectin remained at a low level and was localized to the osteoblast layer and the osteocyte lacunae. Osteopontin mRNA levels increased rapidly in neonatal calvariae. After birth, osteonectin and fibronectin were mainly associated with blood vessels. Thus, fibronectin is one of the earliest **matrix** proteins expressed in calvariae and is rapidly followed by type I collagen, bone sialoprotein, and alkaline phosphatase. Osteocalcin, osteonectin, and osteopontin mRNAs have similar patterns of expression in the developing fetal calvaria, and their synthesis coincided with mineralization.
REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 21 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:640758 HCAPLUS
DOCUMENT NUMBER: 127:298790
TITLE: Bioactive material substrate for enhanced cellular attachment and function
INVENTOR(S): Garcia, Andres J.; Ducheyne, Paul; Boettiger, David
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735000	A1	19970925	WO 1997-US4095	19970318
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2248769	AA	19970925	CA 1997-2248769	19970318
AU 9723269	A1	19971010	AU 1997-23269	19970318
EP 891421	A1	19990120	EP 1997-915983	19970318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

JP 2000506738	T2	20000606	JP 1997-533567		19970318
US 6413538	B1	20020702	US 2000-648098		20000825
PRIORITY APPLN. INFO.:			US 1996-617069	A	19960318
			WO 1997-US4095	W	19970318
			US 1999-253997	B1	19990222

AB Novel noncryst., porous bioactive glass and ceramic materials that permit the in vitro formation of bone tissue when exposed to a tissue culture medium and inoculated with cells are disclosed. The bioactive glass materials may be treated such that when the glass is in contact with anchorage-dependent cells, there is enhanced cell attachment and cell function. Expeditious tissue growth occurs in vitro or in vivo. The glass material is preferably formed from SiO2, CaO, Na2O, and P2O5, although other oxides may be included, and is preferably prepared by melting the constituents, cooling and pulverizing the resulting glass, and then forming and hot-pressing the powder. The glass may be formed to produce templates that are useful for various indications, as well as granules that may be formed into a paste. Thus, a glass containing SiO2 45, Na2O 24.5, CaO 24.5, and P2O5 6 weight% was prepd.from Na2CO3, CaCO3, Ca10(OH)2(PO4)6, and SiO2 by melting at 1350°, pouring into deionized water to produce a glass frit, drying, crushing, grinding to a powder with particle size 40-70 μm, mixing with 2-3% CaCO3 as foaming agent, and hot-pressing into disks under vacuum at .apprx.50 MPa and 460° for .apprx.2 h; the resulting pore size was 70-200 μm. The surface of the glass disks was conditioned for cell attachment and extracellular **matrix** deposition by soaking in a modified Tris buffer solution (pH 6.84) containing ions at concns. similar to those found in interstitial fluid for 48 h, followed by immersion in tissue culture medium containing 20 mM Hepes buffer to stabilize the pH at 7.6 in the pores and at the glass surface. This surface treatment produced a Ca phosphate-rich reaction layer which gradually matured into a poorly crystallized, defective Ca hydroxylapatite layer which incorporated organic biomols. from the culture medium. On inoculation of such treated porous glass disks with neonatal rat calvaria osteoblasts, the disks were totally invaded by the cells and the extracellular **matrix** they elaborated; bonelike sheets were formed throughout the entire thickness of the porous glass.

L136 ANSWER 22 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1997:389582 HCAPLUS
DOCUMENT NUMBER:	127:119818
TITLE:	The binding ability to **matrix** proteins and the inhibitory effects on cell adhesion of synthetic peptides derived from a conserved sequence of osteoblastic integrins
AUTHOR(S):	Liu, Yin Kun; Nemoto, Atsuko; Feng, Yan; Uemura, Toshimasa
CORPORATE SOURCE:	Bionic Design Group, Natl. Inst. Adv. Interdisciplinary Res. (NAIR), Tsukuba Res. Cent., Ibaraki, 305, Japan
SOURCE:	Journal of Biochemistry (Tokyo) (1997), 121(5), 961-968 CODEN: JOBIAO; ISSN: 0021-924X
PUBLISHER:	Japanese Biochemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The β peptide (113-125), derived from a conserved sequence of the β subunit of integrins, was synthesized to investigate its adhesive properties to **matrix** proteins and the effects on cell adhesion to immobilized fibronectin. In this study, we observed that the biotinylated β peptide was able to bind efficiently to immobilized fibronectin, fibrinogen, collagen Type I and vitronectin with different degrees of

affinity. It was also demonstrated that biotinylated fibronectin or fibrinogen could bind to the coated β peptide. This kind of binding, which might be non-covalent linkage, was partially blocked by coincubation with the peptide GRGDS or EDTA, but not by SDGRG. Cell adhesion expts. were performed to study the effect of the β peptide. The data showed that the β peptide partially inhibited both fibroblast L929 and MC3T3-E1 osteoblastic cells from adhering to immobilized fibronectin in a dosage-dependent manner. In the presence of 100 μM concentration of the β peptide, the inhibition rate of cell adhesion was 34% for fibroblast L929 cells and 54.1% for MC 3T3-E1 osteoblastic cells. This research suggests that the β peptide might act independently as an adhesive region of the β subunit of integrins and may occupy the cell-binding site within fibronectin.

L136 ANSWER 23 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:48607 HCAPLUS
DOCUMENT NUMBER: 128:126468
TITLE: Attachment characteristics and involvement of integrins in adhesion of breast cancer cell lines to extracellular bone **matrix** components
AUTHOR(S): van der Pluijm, Gabri; Vloedgraven, Hans; Papapoulos, Socrates; Lowik, Clemens; Grzesik, Wojtek; Kerr, Janet; Robey, Pamela Gehron
CORPORATE SOURCE: Dep. Endocrinology, Univ. Hospital, Leiden, Neth.
SOURCE: Laboratory Investigation (1997), 77(6), 665-675
CODEN: LAINAW; ISSN: 0023-6837
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Evidence is mounting that changes in the ability of cancer cells to adhere to extracellular **matrixes** play a decisive role in metastatic spread. The mechanism underlying the preference of breast cancer cells to metastasize to bone is, however, poorly understood. The authors investigated the expression and involvement of integrin adhesion receptors in the adhesion of breast cancer cells to bone **matrix** (constituents) in two in vitro attachment assays using RGD peptides and anti-integrin antibodies. Breast cancer cells adhered rapidly to extracellular bone **matrix**. Adhesion of most cells to vitronectin, fibronectin, thrombospondin, osteopontin, and the fairly bone-specific bone sialoprotein was inhibited by the 200 μg/mL GRGDS peptide. These data suggest that integrin adhesion receptors can modulate the attachment of breast cancer cells to bone **matrix** mols. In accordance with these findings, the authors found that α1-α5(β1) and αv(β3) integrins were expressed by mammary carcinoma cells. Highly tumorigenic MDA-MB-231 cells, which form osteolytic metastases in vivo, expressed relatively high levels of α2β1, α3β1, α5β1, αvβ3 integrins, when compared to MCF-7, T47D, and ZR75-1 breast cancer cells. Addition of function-blocking anti-α2β1, -α3β1, -α5β1, and -αvβ3 antibodies significantly inhibited the adhesion of MDA-MB-231 breast cancer cells to bone **matrixes**. In conclusion, the data suggest a possible role for β1 and β3 integrin subfamily members in the establishment of skeletal metastases in advanced breast cancer patients. Clearly, functional evidence is required to understand the mechanisms involved in the development of skeletal metastases in breast cancer patients.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L136 ANSWER 24 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:333172 HCAPLUS
DOCUMENT NUMBER: 122:96751
TITLE: Glucocorticoids inhibit the attachment of osteoblasts to bone extracellular **matrix** proteins and decrease β1-integrin levels
AUTHOR(S): Gronowicz, Gloria A.; McCarthy, Mary-Beth
CORPORATE SOURCE: Department of Orthopedics, Univ. of Connecticut Health Center, Farmington, CT, 06032, USA
SOURCE: Endocrinology (1995), 136(2), 598-608
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study, the effect of glucocorticoids on osteoblast adhesion to bone **matrix** proteins and integrin expression was examined in primary rat osteoblasts and a transformed rat osteosarcoma-derived cell line ROS 17/2.8. After 24 h of treatment with corticosterone, these cells displayed a concentration-dependent decrease in adhesion to type I collagen and fibronectin. Adhesion was significantly decreased as early as 4 h after glucocorticoid administration. With 100 nM corticosterone treatment for 24 h, inhibition of the adhesion of ROS 17/2.8 cells and primary osteoblasts to fibronectin was 75% and 50%, and inhibition of adhesion to collagen was 31% and 65%, resp. This effect was specific for osteoblasts, because glucocorticoids did not change the adhesion of fibroblasts. However, glucocorticoids did inhibit the adhesion of all cell types to rat osteonectin. To determine whether the change in osteoblast attachment to collagen and fibronectin was due to an alteration in integrin levels, the plasma membranes of these cells were labeled with [125I]lactoperoxidase, solubilized, and immunopptd. with an antibody to β1. A 24-h treatment with 100 nM corticosterone caused 80% and 64% decreases in β1 levels in primary osteoblasts and ROS 17/2.8 cells, resp. These results were confirmed with immunofluorescence microscopy, which showed a glucocorticoid-induced decrease in β1 staining. Treatment of primary rat osteoblasts and ROS 17/2.8 cells for 72 h with corticosterone also decreased β1-integrin mRNA levels in a dose-dependent manner. Treatment of primary rat osteoblasts and ROS 17/2.8 cells for 72 h with corticosterone also decreased β1-integrin mRNA levels in a dose-dependent manner. These data suggest that integrin modulation may influence osteoblast function and bone formation and, thus contribute to glucocorticoid-induced osteoporosis.

L136 ANSWER 25 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:303816 HCAPLUS
DOCUMENT NUMBER: 122:77572
TITLE: The influence of type I collagen on the development and maintenance of the osteoblast phenotype in primary and passaged rat **calvarial** osteoblasts: modification of expression of genes supporting cell growth, adhesion, and extracellular **matrix mineralization**
AUTHOR(S): Lynch, Maureen P.; Stein, Janet L.; Stein, Gary S.; Lian, Jane B.
CORPORATE SOURCE: Dep. of Cell Biology and Cancer Center, Univ. of Massachusetts Medical Center, Worcester, MA, 01655, USA
SOURCE: Experimental Cell Research (1995), 216(1), 35-45
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Osteoblasts derived from Day 21 fetal rat calvaria grown on films of collagen type I exhibit an earlier and enhanced expression of the differentiated phenotype, compared to cells cultured on plastic. The temporal expression of genes characterizing three distinct periods of growth and differentiation are dramatically modified. During the initial proliferation period, expression of genes normally expressed at high levels on plastic (fibronectin, β1 integrin, and actin) was decreased from 50 to 70% in cells grown on collagen. Genes normally expressed at maximal levels in the postproliferative period (osteonectin, osteocalcin, and osteopontin) were up-regulated severalfold very early. Alkaline phosphatase enzyme activity was elevated 2- to 3-fold during the proliferation period, while mRNA levels remained low, suggesting post-transcriptional modifications. The most dramatic consequence of culture of cells on collagen is the accelerated and uniform mineralization of the **matrix** in contrast to the focal mineralization confined to bone nodules in cultures on plastic. Type I collagen supports maintenance of osteoblast phenotypic properties of passaged cells in the absence of glucocorticoid supplementation required for differentiation of osteoblasts subcultivated on plastic. Treatment of proliferating rat osteoblasts on plastic with 1,25(OH)2D3 blocks osteoblast differentiation and **matrix** mineralization. Although differentiation-related genes (alkaline phosphatase and osteocalcin) were up-regulated by vitamin D, culture on the collagen **matrix** could not overcome the inhibition of mineralization. Taken together, these studies define the critical role of type I collagen in mediating the signaling cascade for expression of a mature osteoblast phenotype and mineralization of the extracellular **matrix** in a physiol. manner.

L136 ANSWER 26 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:405708 HCAPLUS
DOCUMENT NUMBER: 121:5708
TITLE: Bone **matrix** RGD glycoproteins: Immunolocalization and interaction with human primary osteoblastic bone cells in vitro
AUTHOR(S): Grzesik, Wojciech J.; Robey, Pamela Gehron
CORPORATE SOURCE: Natl. Inst. Dent. Res., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Journal of Bone and Mineral Research (1994), 9(4), 487-96
CODEN: JBMREJ; ISSN: 0884-0431
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interaction of cells with extracellular **matrix** is essential for their anchorage, proliferation, migration, and differentiation. In bone **matrix** there are multiple glycoproteins that contain the integrin-binding RGD sequence: fibronectin (FN), thrombospondin (TSP), osteopontin (OPN), bone sialoprotein (BSP), type I collagen (COLL I), and vitronectin (VN). In this study, the localization of TSP, FN, VN, and several integrins within developing human long bone using immunohistochem. methods was examined, as was the effect of all bone RGD proteins on the adhesion of human osteoblastic cells. Thrombospondin, fibronectin, and vitronectin showed distinct localization patterns within bone tissue. TSP was found mainly in osteoid and the periosteum; VN appeared to be present mainly in mature bone **matrix**. FN was present in the periosteum as well as within both mature and immature bone **matrix**. Using a panel of antiintegrin antibodies the authors found that bone cells in vivo and in vitro express α4, αv, α5β1, αvβ3, and β3/β5 integrins, and these receptors are for the most part expressed on all bone cells at different stages of maturation with quant. rather than qual. variations, with the exception of α4, which is

expressed mainly by osteoblasts. Cell attachment assays were performed using primary human cells of the osteoblastic lineage under serum-free conditions. COLL I, TSP, VN, FN, OPN, and BSP promoted bone cell attachment in a dose-dependent manner and were equivalent in action when used in equimolar concns. In the presence of GRGDS peptide in the medium, the adhesion to BSP, OPN, and VN was almost completely blocked (10, 10, and 15% of control, resp.), and attachment to FN, COLL I, and TSP was only slightly decreased (80, 75, and 55%, resp.). These results suggest that human bone cells may use RGD-independent mechanisms for attachment to the latter glycoproteins.

L136 ANSWER 27 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:405870 HCAPLUS
DOCUMENT NUMBER: 119:5870
TITLE: Interactions between the bone **matrix** proteins osteopontin and bone sialoprotein and the osteoclast integrin αvβ3 potentiate bone resorption
AUTHOR(S): Ross, F. Patrick; Chappel, Jean; Alvarez, Jose I.; Sander, Diane; Butler, William T.; Farach-Carson, Mary C.; Mintz, Keith A.; Robey, Pamela Gehron; Teitelbaum, Steven L.; Cheresh, David A.
CORPORATE SOURCE: Med. Cent., Washington Univ., St. Louis, MO, 63110, USA
SOURCE: Journal of Biological Chemistry (1993), 268(13), 9901-7
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have investigated the mechanism by which osteoclasts adhere to and resorb bone. It is shown that these cells express β1 and β3 integrins which are involved in attachment to purified bone **matrix** proteins. Binding to osteopontin and bone sialoprotein is mediated by αvβ3, whereas a β1 integrin is responsible for attachment to fibronectin. Both the rapid attachment by osteoclasts to intact bone particles and their subsequent resorption are blocked by a monoclonal antibody directed to the αvβ3 complex but not by an antibody against β1 integrins. Attachment of osteoclasts to bone is also inhibited with soluble osteopontin, Arg-Gly-Asp-containing peptides derived from both osteopontin and bone sialoprotein, or a monospecific polyclonal antibody against osteopontin. Thus, both osteoclast adherence to bone and subsequent resorption of its **matrix** are dependent on interactions between the bone **matrix** proteins osteopontin and/or bone sialoprotein and the integrin αvβ3. Moreover, collagen, which constitutes 90% of its organic **matrix**, is minimally involved in binding of chicken osteoclasts to bone.

L136 ANSWER 28 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:630922 HCAPLUS
DOCUMENT NUMBER: 117:230922
TITLE: An osteonectin-like protein in the **matrix** of cultured osteogenic cell-line MC3T3-E1, which is associated with calcification
AUTHOR(S): Mizuno, Morimichi; Zhou, Hai Yan; Yamada, Hisashi; Kawamura, Masaaki; Hirano, Hisashi; Kuboki, Yoshinori
CORPORATE SOURCE: Sch. Dent., Hokkaido Univ., Sapporo, Japan
SOURCE: Calcified Tissue International (1992), 51(2), 156-61
CODEN: CTINDZ; ISSN: 0171-967X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Time-dependent changes of the [3H]-proline-labeled noncollagenous proteins synthesized by the osteogenic cell-line MC3T3-E1 were analyzed over a range starting from cell confluency to 13 days after confluency during which time cells formed a bone-like structure. It was found that a 40-kDa protein on SDS-PAGE remarkably increased in the cell-**matrix** layer at about 9 days after cell confluency, just before calcification. This protein was highly purified and was found to contain high amts. of glutamic acid, glycine, and serine. An internal amino acid sequence of this protein was revealed to be K-X-M-A-P-E-E-X-P, which showed homol. with the sequence of the EF-hand domain in osteonectin/**SPARC** (**secreted protein**, acidic, and rich in **cysteine**). This protein co-migrated with collagen in gel filtration and ion-exchange chromatog. Furthermore, it showed high affinity to type I collagen.

L136 ANSWER 29 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:222099 HCAPLUS
DOCUMENT NUMBER: 114:222099
TITLE: Effects of **transforming** growth factor-β on normal clonal bone cell populations
AUTHOR(S): Ber, Rebecca; Kubota, Takao; Sodek, Jaro; Aubin, Jane E.
CORPORATE SOURCE: Med. Res. Counc. Group Periodontal Physiol., Univ. Toronto, Toronto, ON, M5S 1A8, Can.
SOURCE: Biochemistry and Cell Biology (1991), 69(2-3), 132-40
CODEN: BCBIEQ; ISSN: 0829-8211
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Clonal populations of bone cells were isolated to examine more precisely the effects of transforming growth factor-β (TGF-β) on individual subpopulations. Several clonal populations were isolated by limiting dilution from cells derived from 21-day-old fetal rat calvaria. Two of these clones, RCA 11 and RCB 2, were used here. While the two clones responded similarly to parathyroid hormone (PTH) and isoproterenol (ISP) with increases in intracellular cAMP, PGE2 elicited a 10-fold higher response in RCB 2 cells compared with RCA 11. RCB 2 cells expressed a 10-fold higher alkaline phosphatase activity compared with RCA 11. Both clones synthesized a variety of bone **matrix** associated proteins, but only RCA 11 synthesized SPP-1 (osteopontin) constitutively. TGF-β stimulated growth of RCB 2 cells after 24 and 48 h of treatment, but had no effect on growth of RCA 11. TGF-β supported anchorage-independent growth of RCB 2 cells, but not that of RCA 11. At 24-h exposure to TGF-β decreased cAMP responsiveness to PTH and ISP slightly in both clones, but had no effect on PGE2 responses. Significant redns. in alkaline phosphatase activity were seen in both clones after 24- and 48-h treatments with TGF-β. Total protein synthesis as measured by [35S]methionine incorporation was stimulated in both clones, but TGF-β selectively stimulated type I collagen compared with type III collagen. **SPARC** (osteonectin) and secreted phosphoprotein 1 (SSP-1; osteopontin) were stimulated by TGF-β in both RCA 11 and RCB 2 cells. Thus, individual clonal populations of cells within bone may be modulated differentially by TGF-β.

L136 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:140721 HCAPLUS
DOCUMENT NUMBER: 114:140721
TITLE: Heterotopic bone formation in tumor stromal tissue-immunohistochemical considerations
AUTHOR(S): Kumasa, Shunsuke; Mori, Hiromitsu; Mori, Masahiko; Shibutani, Toshiaki; Iwayama, Yukio; Tsujimura,

Takahiro; Ohnishi, Tomokazu; Arakaki, Naokatsu; Nakata, Minoru; Kurisu, Kojiro
CORPORATE SOURCE: Sch. Dent., Asahi Univ., Gifu, 501-02, Japan
SOURCE: Acta Histochemica et Cytochemica (1990), 23(4), 427-39
CODEN: ACHCBO; ISSN: 0044-5991
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ectopic bone forming tumors, calcifying epithelioma Malherbe (6), renal cell carcinoma (1), thyroid adenocarcinoma (1), and ovary carcinoma (1), were examined The process of ectopic bone formation could be classified into 1) bone formation related to epithelial tissue as found in calcifying epithelioma of Malherbe, 2) bone formation from perivascular smooth muscle, and 3) that due to metaplasia occurring in stromal connective tissue of epithelial tumors. Immunohistochem. detection of proteoglycans (PG) was made in bone-forming **matrix** areas, and these areas were pos. for chondroitin 4 and 6 sulfate, and dermatan and heparan sulfate PGs. Immunohistochem., fibronectin, collagen III and bone sialoprotein as **matrix** proteins, and carbonic anhydrase as calcification marker were tested and they appeared in these pre-calcifying tissues.

L136 ANSWER 31 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:165195 HCAPLUS
DOCUMENT NUMBER: 108:165195
TITLE: Differential effects of **transforming** growth factor-β on the synthesis of extracellular **matrix** proteins by normal fetal rat **calvarial** bone cell populations
AUTHOR(S): Wrana, Jeffrey L.; Maeno, Masao; Hawrylyshyn, Brigitte; Yao, Kam Ling; Domenicucci, Carmelo; Sodek, Jaro
CORPORATE SOURCE: Fac. Dent., Univ. Toronto, Toronto, ON, M5S 1A8, Can.
SOURCE: Journal of Cell Biology (1988), 106(3), 915-24
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To determine the effects of transforming growth factor-β (TGF-β) on the different cell types that exist in bone, cell populations (I-IV), progressively enriched in osteoblastic cells relative to fibroblastic cells, were prepared from fetal rat calvaria using timed collagenase digestions. In all populations the synthesis of secreted proteins increased 2-3.5-fold. In particular, collagen, fibronectin, and plasminogen activator inhibitor synthesis was stimulated. However, different degrees of stimulation of individual proteins were observed both within and between cell populations. A marked preferential stimulation of plasminogen activator inhibitor was observed in each population, together with a slight preferential stimulation of collagen, especially type I. In contrast, the synthesis of **SPARC** (**secreted protein** acidic rich in **cysteine**/osteonectin) was stimulated approx. 2-fold by TGF-β, but only in fibroblastic populations. Collectively, these results demonstrate that TGF-β stimulates **matrix** production by bone cells and, through differential effects on individual **matrix** components, may also influence the nature of the **matrix** formed by different bone cell populations. The differential effects of TGF-β on bone cell populations are likely to be important in bone remodeling and fracture repair.

L136 ANSWER 32 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003486180 EMBASE
TITLE: Bone Tissue **Engineering** by Primary

Osteoblast-Like Cells in a Monolayer System and 3-Dimensional Collagen Gel.

AUTHOR: Wiesmann H.P.; Nazer N.; Klatt C.; Szuwart T.; Meyer U.
CORPORATE SOURCE: Dr. H.P. Wiesmann, Klin./Poliklin. Mund/Kief.-Gesichts., Universitatsklinikum Munster, Waldeyerstr 30, D-48149 Munster, Germany. wiesmap@uni-muenster.de

SOURCE: Journal of Oral and Maxillofacial Surgery, (2003) 61/12 (1455-1462).
Refs: 45
ISSN: 0278-2391 CODEN: JOMSDA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose: To engineer living bone tissue in vitro, bone cells must be multiplied and differentiated in cell culture. **Osteoblasts** are known to be the crucial cells responsible for the bone modeling process. Periosteal-derived **osteoblasts** were therefore cultured for up to 3 weeks in Petri dishes as well as in a 3-dimensional collagen gel. Methods: Proliferation, migration, and differentiation of cells as well as the synthesis of extracellular matrix proteins were monitored during the culture period by histology, electron microscopy, and immunohistochemistry. Mineral formation was investigated by electron diffraction studies and element analysis. Results: **Osteoblasts** proliferated and migrated in Petri dishes as well as in the collagen gel without loss of viability during the whole experimental period. They demonstrated a mature **osteoblast** phenotype as indicated by the synthesis of a bone-like extracellular matrix. They formed an extracellular matrix containing osteocalcin, osteonectin, and newly synthesized collagen type I in both environments. Mineral formation was seen in colocalization with the bone-like extracellular matrix proteins in Petri dishes. Microanalytical investigations revealed a matrix vesicle-mediated mineral formation at early stages of culture. Conclusions: Our cell culture confirmed the ability to multiplicate differentiated and viable **osteoblast**-like cells in 2- and 3-dimensional space. Additionally, bone-like mineralization can be induced by primary **osteoblasts** in monolayer culture. The data suggest that this approach can be used as a tool in bone tissue engineering.
.COPYRGT. 2003 American Association of Oral and Maxillofacial Surgeons.

L136 ANSWER 33 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000348665 EMBASE

TITLE: Integrin-mediated signaling regulates AP-1 transcription factors and **proliferation** in **osteoblasts**.

AUTHOR: Cowles E.A.; Brailey L.L.; Gronowicz G.A.
CORPORATE SOURCE: G.A. Gronowicz, Department of Orthopaedics, MC-1110, Univ. of Connecticut Health Center, Farmington, CT 06032, United States. gronowicz@nsol.uchc.edu

SOURCE: Journal of Biomedical Materials Research, (2000) 52/4 (725-737).
Refs: 78
ISSN: 0021-9304 CODEN: JBMRBG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation

033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Since **osteoblast** proliferation is critical for bone development, the effect of bone extracellular matrix (ECM) proteins on **osteoblast** signaling and proliferation in serum-free medium was investigated. Proliferation was highest in primary rat calvarial **osteoblasts** cells grown on fibronectin but less on type I collagen; osteonectin and poly-L-lysine did not support early proliferation. Fibronectin and type I collagen binding requires integrins, whereas cell adhesion to osteonectin or poly-L-lysine does not involve integrins. Therefore, the role of integrins in **osteoblast** signaling, leading to the induction of AP-1 transcription factors (c-fos and c-jun) which are important in cell proliferation, was studied. c-fos and c-jun message levels were increased at 60 min in **osteoblasts** plated onto fibronectin or collagen, but not in cells on osteonectin or poly-L-lysine. Protein synthesis was not required for c-fos mRNA expression; however, kinase activity was necessary for c-fos induction. In cells plated onto fibronectin, c-fos mRNA levels were controlled by protein kinase C and phosphotyrosine kinase signaling pathways. In contrast, c-fos levels in collagen-adhering cells may involve protein kinase A. The signaling pathway involving the phosphorylation of focal adhesion kinase and mitogen-activated kinases was also shown to be transiently increased in **osteoblasts** on fibronectin and type I collagen, but not in cells on poly-L-lysine. These results demonstrate that **osteoblast** binding to the extracellular matrix through integrins induces c-fos and c-jun, and that both fibronectin and collagen affect these AP-1 transcription factors through protein kinase-sensitive pathways. Thus, **osteoblast** proliferation is modulated differentially by specific ECM components. (C) 2000 John Wiley and Sons, Inc.

L136 ANSWER 34 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 97142087 EMBASE
DOCUMENT NUMBER: 1997142087
TITLE: Bone morphogenesis and modeling: soluble signals **sculpt** osteosomes in the solid state.
AUTHOR: Reddi A.H.
CORPORATE SOURCE: A.H. Reddi, Department of Orthopaedic Surgery, Ctr. for Tissue Regeneration/Repair, University of California, Davis, Sacramento, CA 95817, United States
SOURCE: Cell, (1997) 89/2 (159-161).
Refs: 15
ISSN: 0092-8674 CODEN: CELLB5
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 021 Developmental Biology and Teratology
LANGUAGE: English

L136 ANSWER 35 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 97034502 EMBASE
DOCUMENT NUMBER: 1997034502
TITLE: Tissue transglutaminase and factor XIII in cartilage and bone **remodeling.**
AUTHOR: Aeschlimann D.; Mosher D.; Paulsson M.
CORPORATE SOURCE: Dr. D. Aeschlimann, Division of Orthopedic Surgery, University of Wisconsin, F4/312 Clinical Science Center, 600 Highland Ave., Madison, WI 53792-3228, United States

SOURCE: Seminars in Thrombosis and Hemostasis, (1996) 22/5 (437-443).
Refs: 45
ISSN: 0094-6176 CODEN: STHMBV
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English

AB While it is well established that factor XIII functions in crosslinking of the fibrin clot during blood coagulation and in wound healing, the physiological role of tissue transglutaminase is still unclear. Recent studies suggest that the expression of tissue transglutaminase correlates with (terminal) differentiation of cells and that the enzyme may play a role in extracellular matrix remodeling. In cartilage, tissue transglutaminase expression is restricted to hypertrophic chondrocytes and the enzyme is externalized at a distinct step in the chondrocyte maturation program. Upon activation by Ca2+, the transglutaminase modifies matrix constituents in a way that might predispose the matrix for the subsequent mineralization. Crosslinks of the structure γ-glutamyl-ε-lysine are also abundant in bone matrix, but the transglutaminase expressed by **osteoblasts** and presumably involved in crosslinking of newly formed osteoid is likely to be distinct from both tissue transglutaminase and factor XIII. Matrix proteins thought to be crosslinked by transglutaminases in cartilage and bone matrix include glycoproteins such as osteonectin, osteopontin, fibronectin, fibrillin, and collagens II, III, V, and XI. Expression of the A subunit of factor XIII is restricted to megakaryocytes in the bone marrow cavity, and factor XIIIa is abundant in platelets that probably provide the major source for factor XIII in plasma.

L136 ANSWER 36 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 94370316 EMBASE
DOCUMENT NUMBER: 1994370316
TITLE: Osteonectin in matrix **remodeling**. A plasminogen-osteonectin-collagen complex.
AUTHOR: Kelm Jr. R.J.; Swords N.A.; Orfeo T.; Mann K.G.
CORPORATE SOURCE: Department of Biochemistry, College of Medicine, University of Vermont,Burlington, VT 05405, United States
SOURCE: Journal of Biological Chemistry, (1994) 269/48 (30147-30153).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Osteonectin is an adhesive glycoprotein synthesized constitutively by **osteoblasts**, endothelial cells, and megakaryocytes. Bone-derived and platelet-derived osteonectins differ in their electrophoretic mobility and carbohydrate content, and each displays different affinities for collagen matrices. Both types of osteonectin bind to plasminogen (K(d(app)), of 4.7 ± 1.0 x 10-8 M for bone osteonectin and 1.2 ± 0.1 x 10-7 M for platelet osteonectin). The osteonectin-plasminogen interaction is inhibited by α2- antiplasmin and ε-aminocaproic acid, suggesting that the interaction is mediated through the kringle 1 region of plasminogen. Both osteonectins enhance the rate of

plasmin generation by tissue-type plasminogen activator to approximately the same extent as fibrinogen. Equilibrium binding measurements conducted using total internal reflection fluorescence spectroscopy indicate that plasminogen binds to collagen in the presence of bone osteonectin (K(d) = 1.30 ± 0.1 x 10-7 M). No binding of plasminogen to collagen matrix was detected in the presence of platelet osteonectin or in the absence of bone osteonectin. Bone osteonectin-dependent binding of plasminogen to collagen matrix is reversed by the addition of ε-aminocaproic acid. The ability of both types of osteonectin to bind to and influence plasminogen activation and of bone osteonectin to anchor plasminogen on collagen matrices suggests that osteonectin may play a role in directing extracellular matrix proteolysis.

L136 ANSWER 37 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 92328002 EMBASE
DOCUMENT NUMBER: 1992328002
TITLE: Growth on type I collagen promotes expression of the **osteoglastic** phenotype in human osteosarcoma MG-63 cells.
AUTHOR: Adrianarivo A.G.; Robinson J.A.; Mann K.G.; Tracy R.P.
CORPORATE SOURCE: Department of Biochemistry, University of Vermont,Burlington, VT 05405, United States
SOURCE: Journal of Cellular Physiology, (1992) 153/2 (256-265). ISSN: 0021-9541 CODEN: JCLLAX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Using MG-63 cells as a model system capable of partial **osteoblastic** differentiation, we have examined the effect of growth on extracellular matrix. MG-63 cell matrix and purified type I collagen induced a morphological change characterized by long cytoplasmic processes reminiscent of those seen in osteocytes. Concurrent biochemical changes involving bone marker proteins included increased specific activity of cell-associated alkaline phosphatase and increased secretion of osteonectin (up to 2.5-fold for each protein); all changes occurred without alterations in the growth kinetics of the MG-63 cells. The increase in alkaline phosphatase activity was maximal on days 6-8 following seeding; increased osteonectin secretion was most prominent immediately following seeding; all changes decreased as cells reached confluence. Growing cells on type I collagen resulted in an increased induction of alkaline phosphatase activity by 1,25(OH)2D3 (with little change in the 1,25(OH)2D3 induction of osteonectin and osteocalcin secretion), and increased TGF-β induction of alkaline phosphatase activity as well (both TGF-β1 and TGF-β2). Both the 1,25(OH)2D3 and TGF-β effects appeared to be synergistic with growth on type I collagen. These studies support the hypothesis that bone extracellular matrix may play an important role in **osteoblastic** differentiation and phenotypic expression.

L136 ANSWER 38 OF 48 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:432244 BIOSIS
DOCUMENT NUMBER: PREV200300432244
TITLE: Enhancement of **fibronectin**- and **vitronectin**-adsorption to polymer/hydroxyapatite **scaffolds** suppresses the apoptosis of osteoblasts.
AUTHOR(S): Woo, K. M. [Reprint Author]; Wei, G. [Reprint Author]; Ma, P. X. [Reprint Author]

CORPORATE SOURCE: Biologic and Materials Sciences, University of Michigan, Ann Arbor, MI, USA
SOURCE: Journal of Bone and Mineral Research, (September 2002) Vol. 17, No. Suppl 1, pp. S407. print.
Meeting Info.: Twenty-Fourth Annual Meeting of the American Society for Bone and Mineral Research. San Antonio, Texas, USA. September 20-24, 2002. American Society for Bone and Mineral Research.
ISSN: 0884-0431 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003

L136 ANSWER 39 OF 48 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:242147 BIOSIS
DOCUMENT NUMBER: PREV200300242147
TITLE: Extracellular **matrix** molecules improve periodontal ligament cell adhesion to **anorganic** bone **matrix**.
AUTHOR(S): Lallier, T. E. [Reprint Author]; Yukna, R.; Moses, R. L.
CORPORATE SOURCE: Department of Cell Biology and Anatomy, Louisiana State University Health Science Center, School of Dentistry, 1100 Florida Avenue, New Orleans, LA, 70119, USA
tlalli@lsuhsc.edu
SOURCE: Journal of Dental Research, (August 2001) Vol. 80, No. 8, pp. 1748-1752. print.
CODEN: JDREAF. ISSN: 0022-0345.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 May 2003
Last Updated on STN: 21 May 2003

AB Bone replacement graft (BRG) materials are used in periodontal therapy to encourage new **bone formation**. Extracellular **matrix** proteins may improve periodontal ligament fibroblast (PDLF) attachment to these materials. We demonstrate that PDLFs adhere well to the extracellular **matrix** (ECM) proteins **fibronectin**, **vitronectin**, laminin, and collagen types I and IV. PDLFs express numerous ECM-receptor integrin subunit transcripts (alpha1, alpha2, alpha3, alpha4, alpha5, alphaV, beta1, beta5, and beta8) at high levels, while others (alpha6, alpha9, alphaV, beta3, beta6, and beta7) are expressed at reduced levels. Despite the fact that PDLFs adhere well to **fibronectin** and collagen type IV bound to plastic, and express integrins that recognize these ECM proteins, they do not attach well to anorganic bovine bone **matrix** (ABM) coated with these same proteins. However, the addition of **vitronectin**, laminin, or collagen type I to these same ABMs substantially increased PDL cell attachment. Thus, selective use of ECM proteins may be clinically useful in promoting cell attachment to ABM and bone regrowth.

L136 ANSWER 40 OF 48 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:203691 BIOSIS
DOCUMENT NUMBER: PREV199395104916
TITLE: Modulation of **vitronectin** receptor-mediated **osteoclast** adhesion by Arg-Gly-Asp peptide **analogs**: A structure-function analysis.
AUTHOR(S): Horton, Michael A. [Reprint author]; Dorey, Elaine L.; Nesbitt, Stephen A.; Samanen, James; Ali, Fadia E.; Stadel, Jeffrey M.; Nichols, Andrew; Greig, Russel; Helfrich, Miep

H.
CORPORATE SOURCE: ICRF Haemopoiesis Res. Group, St. Bartholomew's Hosp., Dominion House, London EC1A 7BE, UK
SOURCE: Journal of Bone and Mineral Research, (1993) Vol. 8, No. 2, pp. 239-247.
CODEN: JBMREJ. ISSN: 0884-0431.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Apr 1993
Last Updated on STN: 23 Apr 1993

AB This study details the investigation of induction of retractile shape change in the **osteoclast** through inhibition of adhesion between **osteoclasts** and **matrix** with (1) peptide analogs bearing an Arg-Gly-Asp (RGD) sequence, (2) antibodies to the integrin alpha-V-beta-3 **vitronectin** receptor, and (3) the RGD-containing snake venom peptide echistatin. **Osteoclast** retraction on dentin has been demonstrated for GRGDSP peptide, in contrast to the inactivity of the analog containing the conservative RGE sequence modification. An **osteoclast** adhesion assay employing rat or chick bone cells and serum-coated glass coverslips as substrate was developed for routine evaluation of inhibition of adhesion. Antibodies F4 and F11 to the beta-3 chain of rat **vitronectin** receptor were effective at submicromolar concentrations in rat **osteoclasts** (IC-50 0.29 and 0.05 mu-M, respectively), whereas MAb 23C6 to human/chick **vitronectin** receptor was somewhat less effective against chick **osteoclasts** (IC-50 1.6 mu-M). A rank order of RGD analog activity (mean IC-50, mu-M) in the serum-coated glass adhesion assay was derived for the linear peptides GRGDSP (201 mu-M), GRGDTP (180 mu-M), Ac-RGDS-NH-2 (84 mu-M), Ac-RGDV-NH-2 (68 mu-M), RGDV (43 mu-M), GRGDS (38 mu-M), and RGDS (26 mu-M). The two most potent short peptides were the cyclic analog SK&F 106760 Ac-S,S-cyclo-(Cys-(N-alpha-Me)Arg-Gly-Asp-Pen)-NH-2 (IC-50 7.0 mu-M), and the Telios peptide H-Gly-S,S-cyclo-(Pen-Gly-Arg-Gly-Asp-Ser-Pro-Cys)-Ala-OH (IC-50 6.6 mu-M). The snake venom peptide echistatin was the most potent substance evaluated in the serum-coated glass assay (IC-50 0.78 nM) employing either rat or chick **osteoclasts**. Specificity control peptides **fibronectin** CS1 (ligand for VLA-4), fibrinogen H12 (alternate ligand for gpIIb/IIIa), and laminin cell binding fragment YIGSR were inactive up to 800 mu-M. Comparison of SK&F 106760 and the Telios peptide as inhibitors of platelet aggregation (IC-50 0.36 and 10.1 mu-M, respectively) and inhibitors of L-8 skeletal muscle cell adhesion to **vitronectin** (IC-50 67.2 and 12.3 mu-M, respectively) suggests that the Telios peptide is nonselective whereas SK&F 106760 may be selective with regard to beta-3 integrins. This study demonstrates that structural modification in RGD peptides and the use of antireceptor antibodies or the venom peptide echistatin yields potent inhibitors of **vitronectin** receptor-mediated adhesion in isolated rat and click **osteoclasts** . It is hoped that further peptide modification will yield improved specificity and thus selective inhibitory effects upon **bone resorption.**

L136 ANSWER 41 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-132758 [13] WPIX
DOC. NO. CPI: C2004-052966
TITLE: **Bioactive** sol-gel solution useful for **repairing** hard and soft tissue defects comprises biocompatible polymer, gelable inorganic base material, and calcium and phosphorous molecular species.

DERWENT CLASS: A96 B04 D16
INVENTOR(S): BRENNAN, A; CUEVAS, B; HATCHER, B M; SEEGERT, C
PATENT ASSIGNEE(S): (BREN-I) BRENNAN A; (CUEV-I) CUEVAS B; (HATC-I) HATCHER B M; (SEEG-I) SEEGERT C; (UYFL) UNIV FLORIDA
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004005533	A2	20040115	(200413)*	EN	74
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW					
US 2004052861	A1	20040318	(200421)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004005533	A2	WO 2003-US21962	20030710
US 2004052861	A1 Provisional	US 2002-395186P	20020710
		US 2003-616884	20030710

PRIORITY APPLN. INFO: US 2002-395186P 20020710; US 2003-616884 20030710

AB WO2004005533 A UPAB: 20040223
NOVELTY - A bioactive sol-gel solution comprising a biocompatible polymer (a), a gelable inorganic base material (b), and at least one calcium and phosphorous molecular species (c), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a bioactive glass composite comprising (a) and (c); and
(2) formation of a bioactive glass involving mixing (a) - (c), and hydrolyzing the mixture.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - For repairing hard and soft tissue defects (claimed).
ADVANTAGE - The solution has a pH of 1 - 7 (preferably 1.2 - 2), viscosity of 1.5 - 6 Pa sec at 25 deg. C, and is stable for at least 30 days at 25 deg. C.
Dwg.0/27

L136 ANSWER 42 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-090729 [09] WPIX
DOC. NO. NON-CPI: N2004-072745
DOC. NO. CPI: C2004-036860
TITLE: Non-immunogenic prosthetic **device** for implantation into vertebrate subject in region between and connecting two of subject's **bones**, comprises biocompatible glycosidase-treated **matrix** material.
DERWENT CLASS: A11 A96 D16 D22 P32
INVENTOR(S): STONE, K R
PATENT ASSIGNEE(S): (CROS-N) CROSSCART INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003105737	A1	20031224	(200409)*	EN	52

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003105737	A1	WO 2003-US17444	20030604

PRIORITY APPLN. INFO: US 2002-388639P 20020614

AB WO2003105737 A UPAB: 20040205
NOVELTY - A non-immunogenic prosthetic device comprises a biocompatible glycosidase-treated **matrix** material. The device **matrix** has an in-vivo outer surface contour the same as that of a region between and connecting two of subject's **bones**.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for making a prosthetic device by preparing immunologically-compatible **matrix** material, and forming the **matrix** material into a device.

USE - The prosthetic device is used for implantation into vertebrate subject in a region between and connecting two of subject's **bones**. It may be a meniscal augmentation device for implantation into segmental defect of a meniscus, e.g. tear; a prosthetic intervertebral disc; a prosthetic ligament comprising aligned, elongated filaments; or a prosthetic articular cartilage device (claimed). It is used to regenerate tissue in a subject.

ADVANTAGE - The inventive device is immunologically compatible.

DESCRIPTION OF DRAWING(S) - The figure is a perspective view of a prosthetic meniscus.

Prosthetic meniscus 10
Central region 12
Distal tip regions 14, 16
Non-immunogenic mesh 20

Dwg.2/8

L136 ANSWER 43 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-845022 [78] WPIX
DOC. NO. NON-CPI: N2003-675459
DOC. NO. CPI: C2003-237311
TITLE: Implant system for **bone** repair or replacement, includes implant containing scaffold with open cell structure, system of interconnected conduits and injection port, and cement.
DERWENT CLASS: A96 B04 D22 P31
INVENTOR(S): LIEBSCHNER, M A K
PATENT ASSIGNEE(S): (UYRI-N) UNIV RICE WILLIAM MARSH
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2003073912 A2 20030912 (200378)* EN 19
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003073912	A2	WO 2003-US6076	20030228

PRIORITY APPLN. INFO: US 2002-360460P 20020228

AB WO2003073912 A UPAB: 20031203
NOVELTY - An implant system has an implant containing a scaffold with an open cell structure, a system of interconnected conduits extending throughout the scaffold, and an injection port in fluid communication with conduit(s); and cement.

DETAILED DESCRIPTION - An implant system has an implant containing a scaffold with an open cell structure, a system of interconnected conduits extending throughout the scaffold, and an injection port in fluid communication with conduit(s); and cement. The cell structure and conduits are configured so that when the implant is implanted in tissue, the cement is introduced in the implant via injection port and flows through the system of conduits and in the tissue.

An INDEPENDENT CLAIM is also included for stabilizing tissue comprising preparing a cavity of a predetermined size in the tissue (236), inserting the implant into the cavity (235), and injecting cement in the implant so that the cement flows through the system of conduits and into tissue surrounding the implant (200) to secure the implant in the tissue. The implant comprises a scaffold with an open cell structure, a system of interconnected conduits extending throughout the scaffold, and an injection port in fluid communication with conduit(s).

USE - For **bone** repair or replacement.

ADVANTAGE - The implant improves tissue stabilization and/or regeneration, and provides structural support to the damaged area. It has integrated features that allow for controlled fusion of the implanted structure to the native tissue. It acts as a scaffold to support and promote the growth of new tissue.

DESCRIPTION OF DRAWING(S) - The figure shows a section view of the **bone** plug implanted in a **bone**.
Implant 200
Bone 234
Cavity 235
Tissue 236
Cortical **bone** layer 238
Dwg.7/10

L136 ANSWER 44 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-554818 [52] WPIX
CROSS REFERENCE: 2002-268901 [31]
DOC. NO. NON-CPI: N2003-440576
DOC. NO. CPI: C2003-149801
TITLE: Osteoimplant for **repairing** and/or treating **bone** comprises coherent aggregate of elongate **bone** particles.

DERWENT CLASS: A96 B07 D22 P32
INVENTOR(S): BODEN, S D; EDWARDS, J T; MANRIQUE, A; RUSSELL, J L; SCARBOROUGH, N L; SHIMP, L A; TRAIANEDES, K
PATENT ASSIGNEE(S): (BODE-I) BODEN S D; (EDWA-I) EDWARDS J T; (MANR-I) MANRIQUE A; (RUSS-I) RUSSELL J L; (SCAR-I) SCARBOROUGH N L; (SHIM-I) SHIMP L A; (TRAI-I) TRAIANEDES K
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003009235	A1	20030109	(200352)*		19

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003009235	A1 Provisional	US 2000-219198P	20000719
	Provisional	US 2001-288212P	20010502
	CIP of	WO 2001-US22853	20010719
		US 2002-137862	20020502

PRIORITY APPLN. INFO: US 2002-137862 20020502; US 2000-219198P 20000719; US 2001-288212P 20010502; WO 2001-US22853 20010719

AB US2003009235 A UPAB: 20030813
NOVELTY - An osteoimplant comprises a coherent aggregate of elongate **bone** particles. The osteoimplant possesses predetermined dimensions and shape.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(a) a method of making an osteoimplant by providing elongate **bone** particles; mixing the elongate **bone** particles with an aqueous wetting agent to provide a fluid composition containing 5-40 volume% swollen, hydrated elongate **bone** particles; introducing the fluid composition into a mold; and removing aqueous wetting agent to provide a coherent aggregate of elongate **bone** particles possessing the dimensions and shape of the osteoimplant;

(b) a method of making a plug for insertion in a cavity of an implant or **bone** defect site by providing a coherent aggregate of elongate **bone** particles; lyophilizing the coherent aggregate of elongate **bone** particles; and forming the coherent aggregate of elongate **bone** particles into the plug before or after carrying out the lyophilizing step;

(c) a method of treating a **bone** defect in which the **bone** defect site possesses at least one cavity, by inserting a plug in the cavity; and

(d) a method of fusing adjacent vertebrae by providing a space between adjacent vertebrae to be fused; and implanting the implant in the space.

ACTIVITY - Osteopathic.

MECHANISM OF ACTION - None given.

USE - For use in an implant, e.g. an intervertebral implant or a fusion cage, for repairing and/or treating **bone** by implanting the osteoimplant at a **bone** repair site, wherein the repaired **bone** is ethmoid, frontal, nasal, occipital, parietal, temporal, mandible, maxilla, zygomatic, cervical vertebra, thoracic vertebra, lumar vertebra, scarum, rib, sternum, clavicle, scapula, humerus, radius, ulna, carpal **bones**, metacarpal **bones**, phalanges, ilium,

ischium, pubis, femur, tibia, fibula, patella, calcaneus, tarsal and metatarsal **bones** (claimed).

ADVANTAGE - The osteoimplant is swellable upon contact with body and/or irrigation fluids. This ensures good **bone** contact at the implant site even where the site is irregularly shaped. The osteoimplant absorbs body fluids and retains its original shape.

DESCRIPTION OF DRAWING(S) - The figure shows a fusion cage whose void space is filled with a plug.

Dwg.3/5

L136 ANSWER 45 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-428512 [40] WPIX
CROSS REFERENCE: 1999-134113 [12]; 2000-558246 [51]; 2004-061526 [06]
DOC. NO. NON-CPI: N2003-342034
DOC. NO. CPI: C2003-113034
TITLE: **Repair** product for regenerating and/or **repairing** both vascular and avascular cartilage lesions, e.g. mensical tissue lesions, comprises cartilage **repair matrix**, and cartilage-inducing composition containing mixture of proteins.
DERWENT CLASS: B04 P32
INVENTOR(S): ATKINSON, B; BENEDICT, J J
PATENT ASSIGNEE(S): (SULZ) SULZER BIOLOGICS INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6511958	B1	20030128	(200340)*		40

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6511958	B1 CIP of	WO 1998-EP5100	19980812
	CIP of	US 1999-250370	19990216
		US 2000-505209	20000216

PRIORITY APPLN. INFO: US 2000-505209 20000216; WO 1998-EP5100 19980812; US 1999-250370 19990216

AB US 6511958 B UPAB: 20040123

NOVELTY - A cartilage repair product (I) comprising a cartilage repair **matrix** and a cartilage-inducing composition contained on or within the **matrix**, is new. The cartilage-inducing composition contains a mixture of proteins comprising a **bone**-derived osteogenic or chondrogenic formulation that contains at least one **bone** morphogenetic protein, and a transforming growth factor beta protein exogenous to the formulation.

DETAILED DESCRIPTION - A cartilage repair product consists of a cartilage repair **matrix** for conforming to a defect in cartilage, and a cartilage-inducing composition contained on or within the **matrix**. The cartilage-inducing composition contains a mixture of proteins comprising a **bone**-derived osteogenic or chondrogenic formulation that contains at least one **bone** morphogenetic protein (BMP), and a transforming growth factor beta (TGF beta) protein exogenous to the formulation. The ratio of exogenous TGF beta protein to total BMP in the mixture is greater than 10:1. The exogenous TGF beta

protein is present in an amount sufficient to increase cartilage induction by the composition over a level of cartilage induction by the **bone** -derived osteogenic or chondrogenic protein in the absence of TGF beta protein.

USE - (I) is useful for regenerating and/or repairing both vascular and avascular cartilage lesions, e.g. mensical tissue lesions including tears and segmental defects (claimed).

ADVANTAGE - (I) enhances quality of repair of the defect in cartilage as compared to the quality of repair in the absence of the product.

Dwg.0/8

ABEX UPTX: 20030624

EXAMPLE - Bovine tendon type I collagen was placed in one syringe, and acetic acid (10 mM) was placed in another syringe. The syringes were coupled, and the contents of each syringe were mixed for more than 4 hours to produce 2% collagen slurry. After overnight incubation, the preparation was placed in molds, frozen at -20degreesC for more than 4 hours, and lyophilized until dry. The resulting sheet (repair product) had a length of 15.5 mm, a width of 4.8 mm and a thickness of 1.2 mm.

L136 ANSWER 46 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-558246 [51] WPIX
CROSS REFERENCE: 1999-134113 [12]; 2003-428512 [40]; 2004-061526 [06]
DOC. NO. CPI: C2000-166225
TITLE: New cartilage repair products for inducing cell ingrowth into bioresorbable material and cell differentiation into cartilage tissue, comprises protein composition and repair **matrix**.
DERWENT CLASS: B04 D22 P32 P34
INVENTOR(S): ATKINSON, B; BENEDICT, J J
PATENT ASSIGNEE(S): (SULZ) SULZER BIOLOGICS INC
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000048550	A2	20000824	(200051)*	EN	100
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000036999	A	20000904	(200103)		
EP 1161201	A2	20011212	(200204)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002537022	W	20021105	(200304)		114

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000048550	A2	WO 2000-US3972	20000216
AU 2000036999	A	AU 2000-36999	20000216
EP 1161201	A2	EP 2000-915782	20000216
		WO 2000-US3972	20000216
JP 2002537022	W	JP 2000-599344	20000216
		WO 2000-US3972	20000216

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000036999	A Based on	WO 2000048550
EP 1161201	A2 Based on	WO 2000048550
JP 2002537022	W Based on	WO 2000048550

PRIORITY APPLN. INFO: US 1999-250370 19990216

AB WO 200048550 A UPAB: 20040123

NOVELTY - A product for repair of cartilage lesions comprises:

(a) a cartilage repair **matrix** that conforms to a defect in the cartilage; and

(b) a cartilage-inducing composition associated with the **matrix** containing a mixture of proteins.

DETAILED DESCRIPTION - A product for repair of cartilage lesions comprises:

(a) a cartilage repair **matrix** that conforms to a defect in the cartilage; and

(b) a cartilage-inducing composition associated with the **matrix** containing a mixture of proteins.

The mixture of proteins comprises:

(i) transforming growth factor beta 1 (TGF beta 1) (0.01-99.99 %), **bone** morphogenic protein (BMP)-2 (0.01-10 %), BMP-3 (0.01-15 %) and BMP-7 (0.01-10 %);

(ii) a **bone**-derived osteogenic or chondrogenic formulation having at least one BMP, and an exogenous TGF beta protein; or

(iii) a TGF beta protein and at least one BMP.

INDEPENDENT CLAIMS are included for:

(1) methods for repair of cartilage lesions comprising implanting and fixing the cartilage repair products into a cartilage lesion; and

(2) a method for repair of segmental cartilage lesions comprising implanting and fixing into a segmental cartilage lesion:

(a) a first product comprising: (i) a cartilage repair **matrix** configured as a sheet; and (ii) a cartilage-inducing composition associated with the **matrix** with a mixture of proteins containing (I); and

(b) a second product comprising a cartilage repair **matrix** configured to replace cartilage removed from the segmental defect; where the first product is implanted between an edge of the lesion and the second product to provide an interface between the lesion and the second product.

USE - The products are useful for implanting and fixing into a cartilage lesion (specifically an articular or meniscal cartilage lesion, or a tear) to regenerate and/or repair cartilage lesions. They are also useful for enhancing blood vessel formation and angiogenesis, producing fibrochondrocytes, inducing cellular infiltration into the product, inducing cellular proliferation, and producing cellular and spatial organization to form a three-dimensional meniscus tissue.

Dwg.0/8

L136 ANSWER 47 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-610941 [52] WPIX
DOC. NO. CPI: C1999-177848
TITLE: Stimulating **bone** formation, useful for preventing osteoporosis.
DERWENT CLASS: B04 D16
INVENTOR(S): CAO, X; CHANG, Z; SHI, X; SONTHEIMER, H J; YE, Z; YANG, X
PATENT ASSIGNEE(S): (UABR-N) UAB RES FOUND
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9951217	A1	19991014	(199952)*	EN	79
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 9934708	A	19991025	(200011)		
NO 2000005022	A	20001204	(200108)		
EP 1075255	A1	20010214	(200111)	EN	
R: BE CH DE DK FR GB IE IT LI NL SE					
US 6197820	B1	20010306	(200115)		
US 6284464	B1	20010904	(200154)		
CN 1310618	A	20010829	(200176)		
JP 2002510620	W	20020409	(200227)		68
US 2002082235	A1	20020627	(200245)		
AU 757105	B	20030130	(200319)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9951217	A1	WO 1999-US7455	19990405
AU 9934708	A	AU 1999-34708	19990405
NO 2000005022	A	WO 1999-US7455	19990405
		NO 2000-5022	20001005
EP 1075255	A1	EP 1999-916373	19990405
		WO 1999-US7455	19990405
US 6197820	B1 Provisional	US 1998-80859P	19980406
		US 1999-292029	19990416
US 6284464	B1 Provisional	US 1998-80859P	19980406
		US 1999-286682	19990405
CN 1310618	A	CN 1999-807021	19990405
JP 2002510620	W	WO 1999-US7455	19990405
		JP 2000-541988	19990405
US 2002082235	A1 Provisional	US 1998-80859P	19980406
	Div ex	US 1999-286682	19990405
		US 2001-943724	20010831
AU 757105	B	AU 1999-34708	19990405

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9934708	A	Based on	WO 9951217
EP 1075255	A1	Based on	WO 9951217
JP 2002510620	W	Based on	WO 9951217
US 2002082235	A1	Div ex	US 6284464
AU 757105	B	Previous Publ.	AU 9934708
		Based on	WO 9951217

PRIORITY APPLN. INFO: US 1998-80859P 19980406; US 1999-292029 19990416; US 1999-286682 19990405; US 2001-943724 20010831

AB WO 9951217 A UPAB: 19991210
NOVELTY - Interaction between a homeobox-containing transcription factor

(htf) or Hox and (preferably) Smad1 removes transcription repression of the htf, allowing induction of genes.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) inducing gene(s) encoding **bone matrix** proteins, comprising inducing an interaction between Smad1 and a htf;

(2) a method for screening for a compound that stimulates **bone** formation, comprising contacting a cell with a candidate compound, and determining the ability of the compound to inhibit binding of Hoxc-8 to a gene, where inhibition results in induction of the gene; and

(3) regulating disease, comprising inhibiting the binding of htf to a disease-regulating gene, where inhibition of binding removes transcriptional repression of the gene by the htf.

ACTIVITY - Osteopathic; cytostatic; cardiant.

MECHANISM OF ACTION - Inhibitor.

USE - The interaction between Smad1 and Hoxc-8 is especially useful for inducing **bone matrix** proteins, especially osteopontin, useful for producing **osteoblast** and/or chondroblast differentiation. This is useful for stimulating **bone** formation, especially in an osteopenic individual to prevent osteoporosis. Smad1 vector constructs were cloned into a tetracycline-regulated expression system, and permanently transfected into **osteoblast** precursor cell line 2T3. Expression of Smad1 stimulated alkaline phosphatase activity (a hallmark in **bone** formation) in a time dependent manner, and induced **bone** mineralization

The interaction is also useful for regulating disease, especially osteoporosis, cancer, cardiovascular disease and neurological disease, and useful for screening for a compound that stimulates **bone** formation, that can be used to prevent osteoporosis (all claimed).

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ABEX UPTX: 19991210

EXAMPLE - Gluathione S-transferase (GST) pulldown experiments were performed with 35S methionine-labeled Hoxc-8 and a GST-Smad1 fusion protein. Hoxc-8 co-precipitated with the purified GST-Smad1 fusion protein, but not with the GST alone.

Hoxc-8 was tested for DNA binding in a gel-shift experiment. Purified GST-Hoxc-8 fusion protein bound it's DNA, but in a competition assay with GST-Smad1 protein added, the Hoxc-8 binding band was inhibited in a dose dependent manner.

L136 ANSWER 48 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1990-213058 [28] WPIX
DOC. NO. CPI: C1990-091992
TITLE: **Culturing** animal cell - using compound **matrix** of collagen and non-collagen material.
DERWENT CLASS: B04 D16
PATENT ASSIGNEE(S): (ADVN) ADVANCE KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 02142469	A	19900531	(199028)*		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 02142469	A	JP 1988-296291	19881125

PRIORITY APPLN. INFO: JP 1988-296291 19881125
AB JP 02142469 A UPAB: 19930928
The process is used to culture animal cells e.g. **bone** blast, fibroblast, etc. in the collagen gel having tri-dimensional structure and comprises including the various protein **matrix** originated from the cells (or tissues) to be cultured, that is, the components of connective tissue generally called non-collagen protein (containing various glycoproteins, **fibronectin, osteonectin** and proteoglycan) and various growth factors in collagen gel.
USE/ADVANTAGE - Animals cells are cultured economically with high efficiency. Culture medium can be exchanged, keeping various growth factors in collagen gel.
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